COLUMBIA UNIVERSITY
* BIOLOGICAL SERIES VOL. IV *

7. Am 20

BIBLIOTHECA · BOSTONIENSIS · MEDICINAE
·SERVAT·ET·DOCET·
FVNDATA MDCCCLXX
EX DONO
Fritz B. Talbot, M.D.

3.15
31407

Digitized by the Internet Archive
in 2010 with funding from
Open Knowledge Commons and Harvard Medical School

http://www.archive.org/details/cellindevelopmenwils2

THE CELL

IN DEVELOPMENT AND INHERITANCE

Columbia University Biological Series.

EDITED BY

HENRY FAIRFIELD OSBORN

AND

EDMUND B. WILSON.

1. FROM THE GREEKS TO DARWIN.
   By Henry Fairfield Osborn, Sc.D. Princeton.
2. AMPHIOXUS AND THE ANCESTRY OF THE VERTEBRATES.
   By Arthur Willey, B.Sc. Lond. Univ.
3. FISHES, LIVING AND FOSSIL. An Introductory Study.
   By Bashford Dean, Ph.D. Columbia.
4. THE CELL IN DEVELOPMENT AND INHERITANCE.
   By Edmund B. Wilson, Ph.D. J.H.U.
5. THE FOUNDATIONS OF ZOÖLOGY.
   By William Keith Brooks.

COLUMBIA UNIVERSITY BIOLOGICAL SERIES. IV.

THE CELL

IN

DEVELOPMENT AND INHERITANCE

BY

EDMUND B. WILSON, PH. D.
PROFESSOR OF ZOÖLOGY, COLUMBIA UNIVERSITY

SECOND EDITION
REVISED AND ENLARGED

> "Natura nusquam magis est tota quam in minimis"
> PLINY

1754
COLUMBIA
1893
UNIVERSITY
PRESS
IN·LITTERIS·LIBERTAS

New York
THE MACMILLAN COMPANY
LONDON: MACMILLAN & CO., LTD.
1902

All rights reserved

8566

COPYRIGHT, 1896,
BY THE MACMILLAN COMPANY.

COPYRIGHT, 1900,
BY THE MACMILLAN COMPANY.

Set up and electrotyped October, 1896. Reprinted September, 1897; September, 1898.

New edition, revised, set up and electrotyped January, 1900; March, 1902.

BOSTON MEDICAL
FEB 26 1910
LIBRARY.

Norwood Press
J. S. Cushing & Co. — Berwick & Smith
Norwood, Mass. U. S. A.

To my Friend

THEODOR BOVERI

PREFACE

This volume is the outcome of a course of lectures, delivered at Columbia University in the winter of 1892–93, in which I endeavoured to give to an audience of general university students some account of recent advances in cellular biology, and more especially to trace the steps by which the problems of evolution have been reduced to problems of the cell. It was my first intention to publish these lectures in a simple and general form, in the hope of showing to wider circles how the varied and apparently heterogeneous cell-researches of the past twenty years have grown together in a coherent group, at the heart of which are a few elementary phenomena, and how these phenomena, easily intelligible even to those having no special knowledge of the subject, are related to the problems of development. Such a treatment was facilitated by the appearance, in 1893, of Oscar Hertwig's invaluable book on the cell, which brought together, in a form well designed for the use of special students, many of the more important results of modern cell-research. I am glad to acknowledge my debt to Hertwig's book; but it is proper to state that the present volume was fully sketched in its main outlines at the time the *Zelle und Gewebe* appeared. Its completion was, however, long delayed by investigations which I undertook in order to re-examine the history of the centrosomes in the fertilization of the egg, — a subject which had been thrown into such confusion by Fol's extraordinary account of the "Quadrille of Centres" in echinoderms that it seemed for a time impossible to form any definite conception of the cell in its relation to inheritance. By a fortunate coincidence the same task was independently undertaken, nearly at the same time, by several other investigators. The concordant results of these researches led to a decisive overthrow of Fol's conclusions, and the way was thus cleared for a return to the earlier and juster views founded by Hertwig, Strasburger, and Van Beneden, and so lucidly and forcibly developed by Boveri.

The rapid advance of discovery in the mean time has made it seem desirable to amplify the original plan of the work, in order to render it useful to students as well as to more general readers; and to this end it has been found necessary to go over a considerable part of the ground already so well covered by Hertwig.[1] This book does not, however, in any manner aim to be a treatise on general histology, or to give an exhaustive account of the cell. It has rather been my endeavour to consider, within moderate limits, those features of the cell that seem more important and suggestive to the student of development, and in some measure to trace the steps by which our present knowledge has been acquired. A work thus limited necessarily shows many gaps; and some of these, especially on the botanical side, are, I fear, but too obvious. On its historical side, too, the subject could be traced only in its main outlines, and to many investigators of whose results I have made use it has been impossible to do full justice.

To the purely speculative side of the subject I do not desire to add more than is necessary to define some of the problems still to be solved; for I am mindful of Blumenbach's remark that while Drelincourt rejected two hundred and sixty-two "groundless hypotheses" of development, "nothing is more certain than that Drelincourt's own theory formed the two hundred and sixty-third."[2] I have no wish to add another to this list. And yet, even in a field where standpoints are so rapidly shifting and existing views are still so widely opposed, the conclusions of the individual observer may have a certain value if they point the way to further investigation of the facts. In this spirit I have endeavoured to examine some of the more important existing views, to trace them to their sources, and in some measure to give a critical estimate of their present standing, in the hope of finding suggestion for further research.

Every writer on the cell must find himself under a heavy obligation to the works of Van Beneden, Oscar Hertwig, Flemming, Strasburger, and Boveri; and to the last-named author I have a special sense of gratitude. I am much indebted to my former student, Mr. A. P. Mathews, for calling my attention to the importance of the recent work of physiological chemists in its bearing on the problems of synthetic metabolism. The views developed in Chapter VII. have been considerably influenced by his suggestions, and this subject will be more fully treated by him in a forthcoming work; but I have endeavoured as far as possible to avoid anticipating his own special conclusions. Among many others to whom I am indebted for kindly suggestion and advice, I must particularly mention my ever helpful friend, Professor Henry F. Osborn, and Professors J. E. Humphrey, T. H. Morgan, and F. S. Lee.

In copying so great a number of figures from the papers of other investigators, I must make a virtue of necessity. Many of the facts could not possibly have been illustrated by new figures equal in value to those of special workers in the various branches of cytological research, even had the necessary material and time been available. But, apart from this, modern cytology extends over so much debatable ground that no general work of permanent value can be written that does not aim at an objective historical treatment of the subject; and I believe that to this end the results of investigators should as far as practicable be set forth by means of their original figures. Those for which no acknowledgment is made are original or taken from my own earlier papers.

---

[1] Henneguy's *Leçons sur la cellule* is received, too late for further notice, as this volume is going through the press.

[2] Allen Thomson.

The arrangement of the literature lists is as follows. A general list of all the works referred to in the text is given at the end of the book (p. 449). These are arranged in alphabetical order, and are referred to in the text by name and date, according to Mark's convenient system. In order, however, to indicate to students the more important references and partially to classify them, a short separate list is given at the end of each chapter. The chapter-lists include only a few selections from the general list, comprising especially works of a general character and those in which reviews of the special literature may be found.

E. B. W.

Columbia University, New York,
July, 1896.

PREFACE TO THE SECOND EDITION

SINCE the appearance of the first edition of this work, in 1896, the aspect of some of the most important questions with which it deals has materially changed, most notably in case of those that are focussed in the centrosome and involve the phenomena of cell-division and fertilization. This has necessitated a complete revision of the book, many sections having been entirely rewritten, while minor changes have been made on almost every page.

In its first form, the work was compressed within limits too narrow for a sufficiently critical treatment of many disputed subjects. It has therefore been considerably enlarged, and upwards of fifty new illustrations have been added. The endeavour has, however, still been made to keep the book within moderate limits, even at some cost of comprehensiveness ; and the present edition aims no more than did the first to cover the whole vast field of cellular biology. Its limitations are, as before, especially apparent in the field of botanical cytology. Here progress has been so rapid that, apart from the difficulty experienced by a zoölogist in the attempt to maintain a due sense of proportion in reviewing the subject, an adequate treatment would have required a separate volume. I have therefore, for the most part, considered the cytology of plants in an incidental way, endeavouring only to bring the more important phenomena into relation with those more fully considered in the case of animals.

The steady and rapid expansion of the literature of the general subject renders increasingly difficult the historical form of treatment and the citation of specific authority in matters of detail. This plan has nevertheless still been followed as far as possible, despite the increased bulk of the book and the encumbrance of the text with references thus occasioned, in the hope that these disadvantages will be outweighed by increased usefulness of the work. I beg the reader to remember, however, that no approach to a complete history of cytology and experimental embryology could be attempted, save in a work of far greater proportions, and that it has been necessary to pass by, or dismiss with very brief mention, many works to which space would gladly have been given.

Recent research has yielded many new results of high interest, conspicuous among them the outcome of experiments on cell-division, fertilization, and regeneration; and they have cleared up many special problems. Broadly viewed, however, the recent advance of discovery has not, in the author's opinion, tended to simplify our conceptions of cell-life, but has rather led to an emphasized sense of the diversity and complexity of its problems. "One is sometimes tempted to conclude," was recently remarked by a well-known embryologist, "that every egg is a law unto itself!" The jest, perhaps, embodies more of the truth than its author would seriously have maintained, expressing, as it does, a growing appreciation of the intricacy of cell-phenomena, the difficulty of formulating their general aspects in simple terms, and the inadequacy of some of the working hypotheses that have been our guides. It is in the full recognition of such inadequacy, when it exists, and of the danger of hasty generalization in a subject so rapidly moving as this, that our best hope of progress lies.

My best thanks are again due to many friends for helpful criticism, suggestion, and other aid; and I am indebted to Professor Ulric Dahlgren for the beautiful preparation imperfectly represented by Fig. 59 (from a direct photograph); to F. Emil, E. M. Van Harlingen, and Dr. G. N. Calkins, for aid in the preparation of new illustrations; and to Messrs. Ginn & Co. for the electrotypes of Figs. 11, 12, and 188, from the Wood's Holl Biological Lectures for 1899.

COLUMBIA UNIVERSITY,
December 7, 1899.

POSTSCRIPT. — Of especial importance for some of the discussions in Chapters I., V., and VII. are Fischer's extensive work on protoplasm (see Literature, I.) and Strasburger's new researches on reduction (see Literature, V.), both received while this volume was in press and too late for more than a passing mention in the text.

MARCH, 1900.

TABLE OF CONTENTS

INTRODUCTION

PAGE
List of Figures xvii
Historical Sketch of the Cell-theory; its Relation to the Evolution-theory. Earlier Views of Inheritance and Development. Discovery of the Germ-cells. Cell-division, Cleavage, and Development. Modern Theories of Inheritance. Lamarck, Darwin, and Weismann 1
Literature 14

CHAPTER I

General Sketch of the Cell

A. General Morphology of the Cell 19
B. Structural Basis of Protoplasm 23
C. The Nucleus 30
  1. General Structure 31
  2. Finer Structure of the Nucleus 37
  3. Chemistry of the Nucleus 41
D. The Cytoplasm 41
E. The Centrosome 50
F. Other Cell-organs 52
G. The Cell-membrane 53
H. Polarity of the Cell 55
I. The Cell in Relation to the Multicellular Body 58
Literature, I. 61

CHAPTER II

Cell-division

A. Outline of Indirect Division or Mitosis 65
B. Origin of the Mitotic Figure 72
C. Details of Mitosis 77
  1. Varieties of the Mitotic Figure 78
    (*a*) The Achromatic Figure 78
    (*b*) The Chromatic Figure 86
  2. Bivalent and Plurivalent Chromosomes 87
  3. Mitosis in the Unicellular Plants and Animals 88
  4. Pathological Mitoses 97

PAGE
D. The Mechanism of Mitosis . . . 100
  1. Function of the Amphiaster . . . 100
    (*a*) Theory of Fibrillar Contractility . . . 100
    (*b*) Other Facts and Theories . . . 106
  2. Division of the Chromosomes . . . 112
E. Direct or Amitotic Division . . . 114
  1. General Sketch . . . 114
  2. Centrosome and Attraction-sphere in Amitosis . . . 115
  3. Biological Significance of Amitosis . . . 116
F. Summary and Conclusion . . . 119
Literature, II. . . . 121

CHAPTER III

THE GERM-CELLS

A. The Ovum . . . 124
  1. The Nucleus . . . 125
  2. The Cytoplasm . . . 130
  3. The Egg-envelopes . . . 132
B. The Spermatozoön . . . 134
  1. The Flagellate Spermatozoön . . . 135
  2. Other Forms of Spermatozoa . . . 142
  3. Paternal Germ-cells of Plants . . . 142
C. Origin of the Germ-cells . . . 144
D. Growth and Differentiation of the Germ-cells . . . 150
  1. The Ovum . . . 150
    (*a*) Growth and Nutrition . . . 150
    (*b*) Differentiation of the Cytoplasm. Deposit of Deutoplasm . . . 152
    (*c*) Yolk-nucleus . . . 155
  2. Origin of the Spermatozoön . . . 160
  3. Formation of the Spermatozoids in Plants . . . 172
E. Staining-reactions of the Germ-nuclei . . . 175
Literature, III. . . . 177

CHAPTER IV

FERTILIZATION OF THE OVUM

A. General Sketch . . . 180
  1. The Germ-nuclei in Fertilization . . . 181
  2. The Achromatic Structures in Fertilization . . . 185
B. Union of the Germ-cells . . . 196
  1. Immediate Results of Union . . . 200
  2. Paths of the Germ-nuclei . . . 202
  3. Union of the Germ-nuclei. The Chromosomes . . . 204
C. The Centrosome in Fertilization . . . 208
D. Fertilization in Plants . . . 215
E. Conjugation in Unicellular Forms . . . 222
F. Summary and Conclusion . . . 229
Literature, IV. . . . 231

CHAPTER V

REDUCTION OF THE CHROMOSOMES, OÖGENESIS AND SPERMATOGENESIS

PAGE
A. General Outline 234
  1. Reduction in the Female. The Polar Bodies 236
  2. Reduction in the Male. Spermatogenesis 241
  3. Weismann's Interpretation of Maturation 243
B. Origin of the Tetrads 246
  1. General Sketch 246
  2. Detailed Evidence 248
C. Reduction without Tetrad-formation 258
D. Some Peculiarities of Reduction in the Insects 271
E. The Early History of the Germ-nuclei 272
F. Reduction in Unicellular Forms 277
G. Maturation of Parthenogenetic Eggs 280
Appendix
  1. Accessory Cells of the Testis 284
  2. Amitosis in the Early Sex-cells 285
H. Summary and Conclusion 285
Literature, V. 287

CHAPTER VI

SOME PROBLEMS OF CELL-ORGANIZATION

A. The Nature of Cell-organs 291
B. Structural Basis of the Cell 293
C. Morphological Composition of the Nucleus 294
  1. The Chromatin 294
    (*a*) Hypothesis of the Individuality of the Chromosomes . . . 294
    (*b*) Composition of the Chromosomes 301
D. Chromatin, Linin, and Cytoplasm 302
E. The Centrosome 304
F. The Archoplasmic Structures 316
  1. Hypothesis of Fibrillar Persistence 316
  2. The Archoplasm Hypothesis 318
  3. The Attraction-sphere 323
G. Summary and Conclusion 327
Literature, VI. 328

CHAPTER VII

SOME ASPECTS OF CELL-CHEMISTRY AND CELL-PHYSIOLOGY

A. Chemical Relations of Nucleus and Cytoplasm 330
  1. The Proteids and their Allies 331
  2. The Nuclein Series 332
  3. Staining-reactions of the Nuclein Series 334

PAGE
B. Physiological Relations of Nucleus and Cytoplasm 341
  1. Experiments on Unicellular Organisms 342
  2. Position and Movements of the Nucleus 346
  3. The Nucleus in Mitosis 351
  4. The Nucleus in Fertilization 352
  5. The Nucleus in Maturation 353
C. The Centrosome 354
D. Summary and Conclusion 358
Literature, VII. 359

CHAPTER VIII

Cell-division and Development

A. Geometrical Relations of Cleavage-forms 362
B. Promorphological Relations of Cleavage 378
  1. Promorphology of the Ovum 378
    (*a*) Polarity and the Egg-axis 378
    (*b*) Axial Relations of the Primary Cleavage-planes 379
    (*c*) Other Promorphological Characters of the Ovum 382
  2. Meaning of the Promorphology of the Ovum 384
C. Cell-division and Growth 388
Literature, VIII. 394

CHAPTER IX

Theories of Inheritance and Development

A. The Theory of Germinal Localization 397
B. The Idioplasm Theory 401
C. Union of the Two Theories 403
D. The Roux-Weismann Theory of Development 404
E. Critique of the Roux-Weismann Theory 407
F. On the Nature and Causes of Differentiation 413
G. The Nucleus in Later Development 425
H. The External Conditions of Development 428
I. Development, Inheritance, and Metabolism 430
J. Preformation and Epigenesis. The Unknown Factor in Development . . 431
Literature, IX. 434

GLOSSARY 437

GENERAL LITERATURE-LIST 449

INDEX OF AUTHORS 471

INDEX OF SUBJECTS 477

LIST OF FIGURES

INTRODUCTION

PAGE

1. Epidermis of larval salamander 3
2. Section of growing root-tip of the onion 4
3. *Amœba Proteus* 5
4. Cleavage of the ovum in *Toxopneustes* 11
5. Diagram of inheritance 13

CHAPTER I

6. Diagram of a cell 18
7. Spermatogonia of salamander 20
8. Group of cells, showing cytoplasm, nucleus, and centrosomes 21
9. Living cells of salamander larva, showing fibrillar structure 24
10. Alveolar or foam-structure of protoplasm, according to Bütschli 26
11. Structure of protoplasm in the echinoderm egg 27
12. Aster-formation in alveolar protoplasm 28
13. Nuclei from the crypts of Lieberkühn 32
14. Special forms of nuclei 35
15. Scattered nucleus in *Trachelocerca* 37
16. Scattered nucleus in Bacteria and Flagellata 39
17. Ciliated cells 43
18. Cells of amphibian pancreas 44
19. Nephridial cell of *Clepsine* 45
20. Nerve-cell of frog 47
21. Diagram of dividing cell 49
22. Diagrams of cell-polarity 56
23. Centrosomes in epithelium and in blood-corpuscles 57

CHAPTER II

24. Remak's scheme of cell-division 64
25. Diagram of the prophases of mitosis 66
26. Diagram of later phases of mitosis 69
27. Prophases in salamander-cells 73
28. Metaphase and anaphases in salamander-cells 75
29. Telophases in salamander-cells 76
30. Mid-body and cell-plate in cells of *Limax* 79
31. Middle phases of mitosis in *Ascaris*-eggs 80
32. Mitosis in *Stypocaulon* 81

FIG. PAGE
33. Mitosis in *Erysiphe* . . . 83
34. Mitosis in pollen-mother-cells of lily, according to Guignard . . . 84
36. Mitosis in spore-cells of *Equisetum* . . . 85
37. Heterotypical mitosis . . . 87
38. Mitosis in Infusoria . . . 89
39. Mitosis in *Euglypha* . . . 90
40. Mitosis in *Euglena* . . . 91
41. Mitosis in *Acanthocystis* . . . 92
42. Mitosis in *Noctiluca* . . . 93
43. Mitosis in *Paramœba* . . . 95
44. Mitosis in *Actinosphærium* . . . 96
45. Mitosis in *Actinosphærium* . . . 97
46. Pathological mitoses in cancer-cells . . . 98
47. Pathological mitosis caused by poisons . . . 99
48. Van Beneden's account of astral systems in *Ascaris* . . . 100
49. Leucocytes . . . 102
50. Pigment-cells . . . 103
51. Heidenhain's model of mitosis . . . 104
52. Mitosis in the egg of *Toxopneustes* . . . 107
53. Pathological mitoses in polyspermy . . . 109
54. Nuclei in the spireme-stage . . . 112
55. Early division of chromatin in *Ascaris* . . . 113
56. Amitotic division . . . 115

CHAPTER III

57. Volvox . . . 123
58. Ovum of *Toxopneustes* . . . 126
59. Ovum of the cat . . . 127
60. Ovum of *Nereis* . . . 129
61. Germinal vesicles of *Unio* and *Epeira* . . . 130
62. Insect-egg . . . 132
63. Micropyle in *Argonauta* . . . 133
64. Germ-cells of *Volvox* . . . 134
65. Diagram of the flagellate spermatozoön . . . 135
66. Spermatozoa of fishes and amphibia . . . 136
67. Spermatozoa of birds and other animals . . . 138
68. Spermatozoa of mammals . . . 140
69. Unusual forms of spermatozoa . . . 141
70. Spermatozoids of *Chara* . . . 142
71. Spermatozoids of various plants . . . 143
72. Germ-cells of *Cladonema* . . . 146
73. Primordial germ-cells of *Ascaris* . . . 147
74. Primordial germ-cells of *Cyclops* . . . 149
75. Ovarian ova and follicles of *Helix* . . . 151
76. Egg and nurse-cells in *Ophryotrocha* . . . 152
77. Ovarian eggs of insects . . . 153
78. Young ovarian eggs of various animals . . . 154
79. Young ovarian eggs of birds and mammals . . . 155
80. Ovarian eggs of spider, earthworm, ascidian, showing yolk-nucleus . . . 157

FIG. PAGE
81. Ovarian eggs of *Limulus* and *Polyzonium* 159
82. Formation of the spermatozoön in *Anasa* 162
83. Transformation of the spermatids of the salamander 164
84. Formation of the spermatozoön in *Salamandra* and *Amphiuma* 166
85. The same in *Helix* and in elasmobranchs 168
86. The same in mammals 169
87. Formation of spermatozoids in cycads 173
88. Formation of spermatozoids in cryptogams 174

CHAPTER IV

89. Fertilization of *Physa* 180
90. Fertilization of *Ascaris* 183
91. Germ-nuclei of Nematodes 184
92. Fertilization of the mouse 185
93. Fertilization of *Pterotrachea* 186
94. Entrance and rotation of sperm-head in *Toxopneustes* 187
95. Conjugation of the germ-nuclei in *Toxopneustes* 189
96. Diagrams of fertilization 190
97. Fertilization of *Nereis* 191
98. Fertilization of *Cyclops* 193
99. Fertilization and persistence of centrosomes in *Thalassema* 195
100. Entrance of spermatozoön into the egg 197
101. Pathological polyspermy 199
102. Polar rings of *Clepsine* 201
103. Paths of the germ-nuclei in *Toxopneustes* 203
104. Fertilization of *Myzostoma* 209
105. Fertilization of *Pilularia* 216
106. Penetration of the pollen-tube in angiosperms 217
107. Fertilization of the lily 219
108. Fertilization in *Zamia* 220
109. Diagram of conjugation in Infusoria 223
110. Conjugation of *Paramœcium* 225
111. Conjugation of *Vorticella* 226
112. Conjugation of *Noctiluca* 227
113. Conjugation of *Spirogyra* 228

CHAPTER V

114. Polar bodies in *Toxopneustes* 234
115. Genesis of the egg 235
116. Diagram of formation of polar bodies 237
117. Polar bodies in *Ascaris* 239
118. Genesis of the spermatozoön 240
119. Diagram of reduction in the male 242
120. Spermatogenesis of *Ascaris* 244
121. Diagrams illustrating tetrad-formation 247
122. Tetrads of *Gryllotalpa* 249
123. Tetrads and polar bodies in *Cyclops* 250

FIG. PAGE
124. Diagrams of tetrad-formation in arthropods 251
125. Germinal vesicles and tetrads 252
126. Maturation in *Anasa* 254
127. Maturation in *Anasa* 255
128. Diagrams of reduction 259
129. Maturation in *Thalassema* 260
130. Maturation in *Thalassema* and *Zirphæa* 261
131. Maturation in *Salamandra* 262
132. The maturation-divisions in angiosperms 264
133. Maturation in *Lilium* 266
134. Maturation in *Lilium* 268
135. Diagrams of reduction in the flowering plants 270
136. Ovary of *Canthocamptus* 273
137. Polar spindles without centrosomes 276
138. Polar bodies in *Actinophrys* 278
139. Polar bodies in *Actinosphærium* 278
140. Conjugation and reduction in *Closterium* 279
141. First type of parthenogenetic maturation in *Artemia* 282
142. Second type of parthenogenetic maturation in *Artemia* 283

CHAPTER VI

143. Abnormalities in the fertilization of *Ascaris* 295
144. Giant embryo of *Ascaris* 296
145. Individuality of chromosomes in *Ascaris* 297
146. Independence of chromosomes in fertilization of *Cyclops* 298
147. Hybrid fertilization of *Ascaris* 300
148. Mitosis with intranuclear centrosome in *Ascaris* 305
149. Abnormal mitoses in *Hemerocallis* 306
150. Centrosomes in *Chætopterus* and *Cerebratulus* 307
151. Artificially produced asters and centrosomes in echinoderms 308
152. Diagram of different types of centrosome and centrosphere 310
153. Polar mitoses in *Diaulula* 312
154. Astral systems in *Unio* 313
155. Astral systems in *Cerebratulus* and *Thalassema* 320
156. Structure of the aster in spermatogonium of salamander 326

CHAPTER VII

157. History of chromosomes in the germinal vesicle of sharks 339
158. Nucleated and enucleated fragments of *Stylonychia* 342
159. Regeneration in *Stentor* 343
160. Nucleated and enucleated fragments of *Amœba* 344
161. Nucleated and enucleated fragments of plant-protoplasm 345
162. Position of nuclei in plant-cells 347
163. Ovary of *Forficula* 349
164. Normal and dwarf larvæ of sea-urchins 352
165. Supernumerary centrosome in *Ascaris* 355
166. Cleavage of dispermic egg of *Toxopneustes* 356
167. Centrosomes and cilia 357

CHAPTER VIII

FIG. PAGE
168. Geometrical relations of cleavage-planes in plants 363
169. Cleavage of *Synapta* 365
170. Cleavage of *Polygordius* 367
171. Cleavage of *Nereis* 369
172. Variations in the third cleavage 370
173. Meroblastic cleavage in the squid 372
174. Rudimentary cells in *Aricia* 373
175. Teloblasts of the earthworm 374
176. Contradiction of Hertwig's rule in *Ascaris* 376
177. Bilateral cleavage in tunicates 380
178. Bilateral cleavage in *Loligo* 381
179. Eggs of *Loligo* 382
180. Eggs and embryos of *Corixa* 383
181. Variations in axial relations of *Cyclops* 385

CHAPTER IX

182. Half-embryos of the frog 400
183. Half and whole cleavage in sea-urchins 407
184. Normal and dwarf gastrulas of *Amphioxus* 408
185. Dwarf and double embryos of *Amphioxus* 409
186. Cleavage of sea-urchin eggs under pressure 411
187. Cleavage of *Nereis*-eggs under pressure 412
188. Diagrams of cleavage in mollusks and polyclades 414
189. Partial larvæ of ctenophores 418
190. Partial cleavage in *Ilyanassa* 420
191. Double embryos of frog 421
192. Cleavage in *Crepidula* 424
193. Normal and modified larvæ of sea-urchins 428
194. Regeneration in cœlenterates 429

BOSTON MEDICAL LIBRARY.
FEB 26 1910

INTRODUCTION

> "*Jedes Thier erscheint als eine Summe vitaler Einheiten,* von denen jede den vollen Charakter des Lebens an sich trägt."
> VIRCHOW.[1]

DURING the half-century that has elapsed since the enunciation of the cell-theory by Schleiden and Schwann, in 1838–39, it has become ever more clearly apparent that the key to all ultimate biological problems must, in the last analysis, be sought in the cell. It was the cell-theory that first brought the structure of plants and animals under one point of view, by revealing their common plan of organization. It was through the cell-theory that Kölliker, Remak, Nägeli, and Hofmeister opened the way to an understanding of the nature of embryological development, and the law of genetic continuity lying at the basis of inheritance. It was the cell-theory again which, in the hands of Goodsir, Virchow, and Max Schultze, inaugurated a new era in the history of physiology and pathology, by showing that all the various functions of the body, in health and in disease, are but the outward expression of cell-activities. And at a still later day it was through the cell-theory that Hertwig, Fol, Van Beneden, and Strasburger solved the long-standing riddle of the fertilization of the egg and the mechanism of hereditary transmission. No other biological generalization, save only the theory of organic evolution, has brought so many apparently diverse phenomena under a common point of view or has accomplished more for the unification of knowledge. The cell-theory must therefore be placed beside the evolution-theory as one of the foundation stones of modern biology.

And yet the historian of latter-day biology cannot fail to be struck with the fact that these two great generalizations, nearly related as they are, have been developed along widely different lines of research, and have only within a very recent period met upon a common ground. The theory of evolution originally grew out of the study of natural history, and it took definite shape long before the ultimate structure of living bodies was in any degree comprehended. The evolutionists of the Lamarckian period gave little heed to the finer details of internal organization. They were concerned mainly with the more obvious characters of plants and animals — their forms, colours, habits, distribution, their anatomy and embryonic development — and with the systems of classification based upon such characters; and long afterward it was, in the main, the study of like characters with reference to their historical origin that led Darwin to his splendid triumphs. The study of microscopical anatomy, on which the cell-theory was based, lay in a different field. It was begun and long carried forward with no thought of its bearing on the origin of living forms; and even at the present day the fundamental problems of organization, with which the cell-theory deals, are far less accessible to historical inquiry than those suggested by the more obvious external characters of plants and animals. Only within a few years, indeed, has the ground been cleared for that close alliance between students of organic evolution and students of the cell, which forms so striking a feature of latter-day biology and is exerting so great an influence on the direction of research. It has, therefore, only recently become possible adequately to formulate the great problems of development and heredity in the terms of cellular biology — indeed, we can as yet do little more than so formulate them. Yet the fact that these two great lines of research, both concerned with the deeper problems of life, yet having their beginnings so far apart, have at length converged to a meeting-point, is one of the more striking evidences of progress that modern biology has to show; and it sufficiently justifies an attempt to treat the cell from the standpoint of the general student of development.

---

[1] *Cellularpathologie*, p. 12, 1858.

Let us at the outset briefly outline the cell-theory as thus regarded, and indicate the manner of its historical connection with the general problems of evolution.[1]

---

[1] Schleiden and Schwann are universally and justly recognized as the founders of the cell-theory; but like every other great generalization the theory was based on a long series of earlier investigations beginning with the memorable microscopical researches of Leeuwenhoek, Malpighi, Hooke, and Grew in the second half of the seventeenth century.

Wolff, in the *Theoria Generationis* (1759), clearly recognized the "spheres" and "vesicles" composing the embryonic parts both of animals and of plants, though without grasping their real nature or mode of origin, and his conclusions were developed by the botanist Mirbel at the beginning of the present century. Nearly at the same time (1805) Oken foreshadowed the cell-theory in the form that it assumed with Schleiden and Schwann; but his conception of "Urschleim" and "Bläschen" can hardly be regarded as more than a lucky guess. A still closer approximation to the truth is found in the works of Turpin (1826), Meyen (1830), Raspail (1831), and Dutrochet (1837); but these, like others of the same period, only paved the way for the real founders of the cell-theory. Among other immediate predecessors or contemporaries of Schleiden and Schwann should be especially mentioned Robert Brown, Dujardin, Johannes Müller, Purkinje, Hugo von Mohl, Valentin, Unger, Nägeli, and Henle. The significance of Schleiden's, and especially of Schwann's, work lies in the thorough and comprehensive way in which the problem was studied, the philosophic breadth with which the conclusions were developed, and the far-reaching influence which they exercised upon subsequent research. In this respect it is hardly too much to compare the *Mikroskopische Untersuchungen* with the *Origin of Species.*

During the past thirty years the theory of organic descent has been shown, by an overwhelming mass of evidence, to be the only tenable conception of the origin of diverse living forms, however we may conceive the causes of the process. While the study of general zoölogy and botany has systematically set forth the results, and in a measure the method, of organic evolution, the study of microscopical anatomy has shown us the nature of the material on which it has operated, demonstrating that the obvious characters of plants and animals are but varying expressions of a subtle interior organization common to all. In its broader outlines the nature of this organization is now accurately determined; and the "cell-theory," by which it is formulated, is, therefore, no longer of an inferential or hypo-

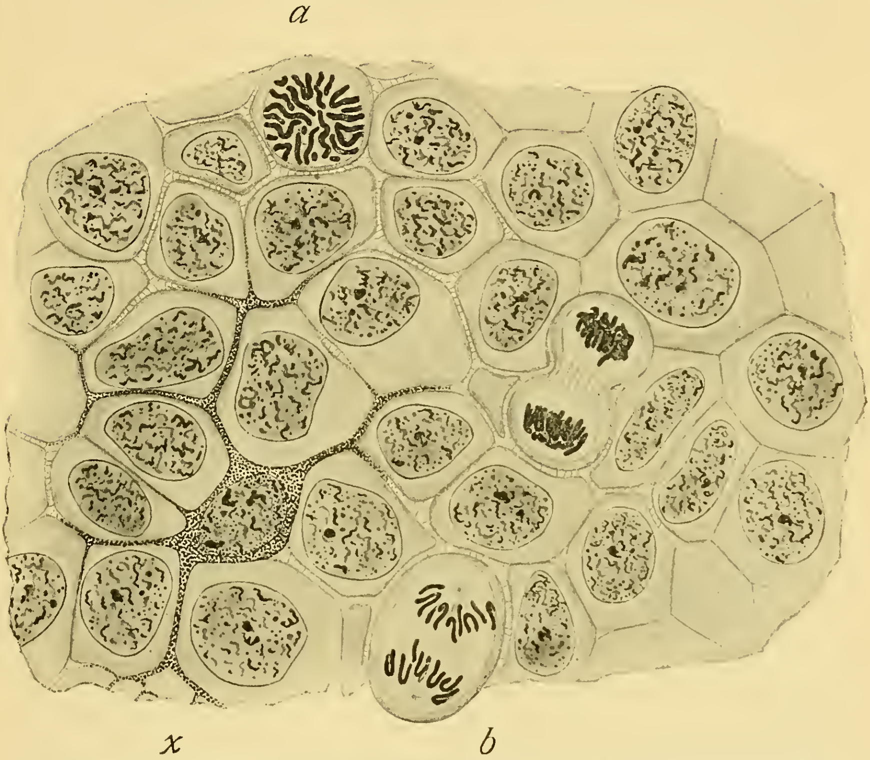

Fig. 1. — A portion of the epidermis of a larval salamander (*Amblystoma*) as seen in slightly oblique horizontal section, enlarged 550 diameters. Most of the cells are polygonal in form, contain large nuclei, and are connected by delicate protoplasmic bridges. Above *x* is a branched, dark pigment-cell that has crept up from the deeper layers and lies between the epidermal cells. Three of the latter are undergoing division, the earliest stage (*spireme*) at *a*, a later stage (mitotic figure in the anaphase) at *b*, showing the chromosomes, and a final stage (*telophase*), showing fission of the cell-body, to the right.

thetical character, but a generalized statement of observed fact which may be outlined as follows: —

In all the higher forms of life, whether plants or animals, the body may be resolved into a vast host of minute structural units known as *cells*, out of which, directly or indirectly, every part is built (Figs. 1, 2). The substance of the skin, of the brain, of the blood, of the bones or muscles or any other tissue, is not homogeneous, as it appears to the unaided eye, but is shown by the microscope to be an aggregate composed of innumerable minute bodies, as if it were a colony or congeries of organisms more elementary than itself. The name *cells* given to these bodies by the early botanists, and ultimately adopted by nearly all students of microscopical anatomy, was not happily chosen; for modern studies have shown that although the cell may assume the form of a hollow chamber, as the name indicates, this is not one of its characteristic or even usual features. Essentially the cell is a minute mass of *protoplasm*, a substance long since identified by Cohn, Leydig, Max Schultze, and De Bary as the essential active basis of the organism, afterward happily characterized

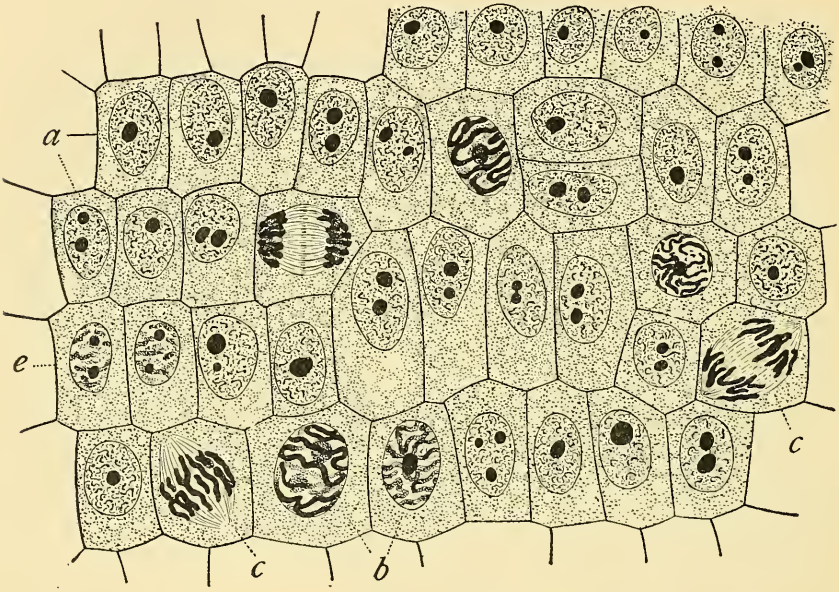

Fig. 2. — General view of cells in the growing root-tip of the onion, from a longitudinal section, enlarged 800 diameters.

a. non-dividing cells, with chromatin-network and deeply stained nucleoli; *b.* nuclei preparing for division (spireme-stage); *c.* dividing cells showing mitotic figures; *e.* pair of daughter-cells shortly after division.

by Huxley as the "physical basis of life," and at the present time universally recognized as the immediate substratum of all vital activity.[1] Endlessly diversified in the details of their form and structure, these protoplasmic masses nevertheless possess a characteristic type of organization common to them all; hence, in a certain sense, they may be regarded as elementary organic units out of which the body is compounded. This composite structure is, however, characteristic of only the higher forms of life. Among the lowest forms at the base of the series are an immense number of microscopic plants and animals, familiar examples of which are the bacteria, diatoms, rhizopods, and Infusoria, in which the entire body consists of a single cell (Fig. 3), of the same general type as those which in the higher multicellular forms are associated to form one organic whole. Structurally, therefore, the multicellular body is in a certain sense comparable with a colony or aggregation of the lower one-celled forms.[2] This com-

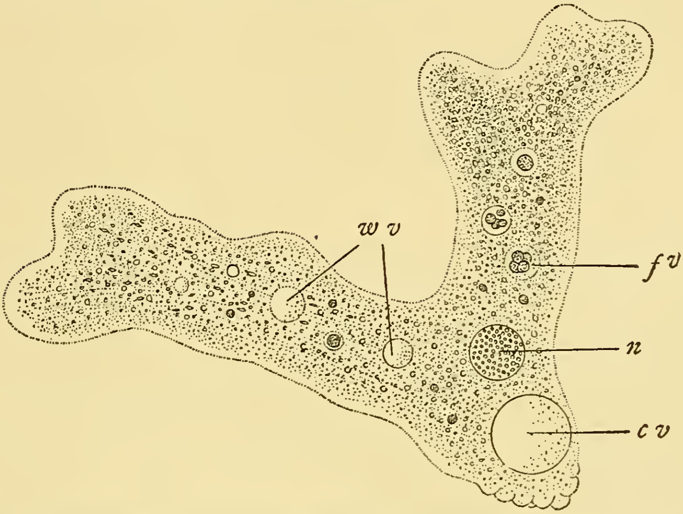

Fig. 3. — *Amœba Proteus*, an animal consisting of a single naked cell, × 280. (From Sedgwick and Wilson's Biology.)

n. The nucleus; *w.v.* water-vacuoles; *c.v.* contractile vacuole; *f.v.* food-vacuole.

---

[1] The word *protoplasm* is due to Purkinje (1840), who applied it to the formative substance of the animal embryo and compared it with the granular material of vegetable "cambium." It was afterward independently used by H. von Mohl (1846) to designate the contents of the plant-cell. The full physiological significance of protoplasm, its identity with the "sarcode" (Dujardin) of the unicellular forms, and its essential similarity in plants and animals, was first clearly placed in evidence through the classical works of Max Schultze and De Bary, beside which should be placed the earlier works of Dujardin, Unger, Nägeli, and Mohl, and that of Cohn, Huxley, Virchow, Leydig, Brücke, Kühne, and Beale.

[2] This comparison must be taken with some reservation, as will appear beyond.

parison is not less suggestive to the physiologist than to the morphologist. In the one-celled forms all of the vital functions are performed by a single cell. In the multicellular forms, on the other hand, these functions are not equally performed by all the cells, but are in varying degree distributed among them, the cells thus falling into physiological groups or tissues, each of which is especially devoted to the performance of a specific function. Thus arises the "physiological division of labour" through which alone the highest development of vital activity becomes possible; and thus the cell becomes a unit, not merely of structure, but also of function. Each bodily function, and even the life of the organism as a whole, may thus in one sense be regarded as a resultant arising through the integration of a vast number of cell-activities; and it cannot be adequately investigated without the study of the individual cell-activities that lie at its root.[1]

The foregoing conceptions, founded by Schwann, and skilfully developed by Kölliker, Siebold, Virchow, and Haeckel, gave an impulse to anatomical and physiological investigation the force of which could hardly be overestimated; yet they did not for many years measurably affect the more speculative side of biological inquiry. The *Origin of Species*, published in 1859, scarcely mentions it; nor, with the important exception of the theory of pangenesis, did Darwin attempt at any later period to bring it into any very definite relation to his views. The initial impulse to the investigations that brought the cell-theory into definite contact with the evolution-theory was given nearly twenty years after the *Origin of Species*, by researches on the early history of the germ-cells and the fertilization of the ovum. Begun in 1873–74 by Auerbach, Fol, and Bütschli, and eagerly followed up by Oscar Hertwig, Van Beneden, Strasburger, and a host of later workers, these investigations raised wholly new questions regarding the mechanism of development and the *rôle* of the cell in hereditary transmission. Through them it became for the first time clearly apparent that the general problems of embryology, heredity, and evolution are indissolubly bound up with those of cell-structure, and can only be fully apprehended in the light of cytological research. As the most significant step in this direction, we may regard the identification of the *cell-nucleus* as the vehicle of inheritance, made independently and almost simultaneously in 1884-85 by Oscar Hertwig, Strasburger, Kölliker, and Weismann,[1] while nearly at the same time (1883) the splendid researches of Van Beneden on the early history of the animal egg opened possibilities of research into the finer details of cell-phenomena of which the early workers could hardly have dreamed.

---

[1] *Cf.* pp. 58–61. "It is to the cell that the study of every bodily function sooner or later drives us. In the muscle-cell lies the problem of the heart-beat and that of muscular contraction; in the gland-cell reside the causes of secretion; in the epithelial cell, in the white blood-cell, lies the problem of the absorption of food, and the secrets of the mind are hidden in the ganglion-cell. . . . If then physiology is not to rest content with the mere extension of our knowledge regarding the gross activities of the human body, if it would seek a real explanation of the fundamental phenomena of life, it can only attain its end through the study of *cell-physiology*" (Verworn, *Allgemeine Physiologie*, p. 53, 1895).

We can only appreciate the full historical significance of the new period thus inaugurated by a glance at the earlier history of opinion regarding embryological development and inheritance. To the modern student the germ is, in Huxley's words, simply a detached living portion of the substance of a preëxisting living body[2] carrying with it a definite structural organization characteristic of the species. By the earlier embryologists, however, the matter was very differently regarded; for their views in regard to inheritance were vitiated by their acceptance of the Greek doctrine of the equivocal or spontaneous generation of life; and even Harvey did not escape this pitfall, near as he came to the modern point of view. "The egg," he says, "is the mid-passage or transition stage between parents and offspring, between those who are, or were, and those who are about to be; it is the hinge or pivot upon which the whole generation of the bird revolves. The egg is the terminus from which all fowls, male and female, have sprung, and to which all their lives tend — it is the result which nature has proposed to herself in their being. And thus it comes that individuals in procreating their like for the sake of their species, endure forever. The egg, I say, is a period or portion of this eternity."[3]

This passage appears at first sight to be a close approximation to the modern doctrine of germinal continuity about which all theories of heredity are revolving. In point of fact, however, Harvey's view is only superficially similar to this doctrine; for, as Huxley pointed out, it was obscured by his belief that the germ might arise "spontaneously," or through the influence of a mysterious "*calidum innatum*," out of not-living matter.[4] Neither could Harvey, great physiologist and embryologist as he was, have had any adequate conception of the real nature of the egg and its morphological relation to the body of which it forms a part, since the cellular structure of living things was not comprehended until nearly two centuries later, the spermatozoön was still undiscovered, and the nature of fertilization was a subject of fantastic and baseless speculation. For a hundred years after Harvey's time embryologists sought in vain to penetrate the mysteries enveloping the beginning of the individual life, and despite their failure the controversial writings of this period form one of the most interesting chapters in the history of biology. By the extreme "evolutionists" or "præformationists" the egg was believed to contain an embryo fully formed in miniature, as the bud contains the flower or the chrysalis the butterfly. Development was to them merely the unfolding of that which already existed; inheritance, the handing down from parent to child of an infinitesimal reproduction of its own body. It was the service of Bonnet to push this conception to its logical consequence, the theory of *emboîtement* or encasement, and thus to demonstrate the absurdity of its grosser forms, pointing out that if the egg contains a complete embryo, this must itself contain eggs for the next generation, these other eggs in their turn, and so *ad infinitum*, like an infinite series of boxes, one within another — hence the term *emboîtement*. Bonnet himself renounced this doctrine in his later writings, and Caspar Friedrich Wolff (1759) led the way in a return to the teachings of Harvey, showing by precise actual observation that the egg does not at first contain any formed embryo whatever; that its structure is wholly different from that of the adult; that development is not a mere process of unfolding, but involves the continual formation, one after another, of new parts, previously non-existent as such. This is somewhat as Harvey, himself following Aristotle, had conceived it — a process of *epigenesis* as opposed to *evolution*. Later researches established this conclusion as the very foundation of embryological science.

---

[1] It must not be forgotten that Haeckel expressed the same view in 1866 — only, however, as a speculation, since the data necessary to an inductive conclusion were not obtained until long afterward. "The internal nucleus provides for the transmission of hereditary characters, the external plasma on the other hand for accommodation or adaptation to the external world" (*Gen. Morph.*, pp. 287-289).

[2] *Evolution in Biology*, 1878; *Science and Culture*, p. 291.

[3] *De Generatione*, 1651; Trans., p. 271.

[4] Whitman, too, in a brilliant essay, has shown how far Harvey was from any real grasp of the law of genetic continuity, which is well characterized as the central fact of modern biology. *Evolution and Epigenesis*, Wood's Holl Biological Lectures, 1894.

But although the external nature of development was thus determined, the actual structure of the egg and the mechanism of inheritance remained for nearly a century in the dark. It was reserved for Schwann (1839) and his immediate followers to recognize the fact, conclusively demonstrated by all later researches, that *the egg is a cell* having the same essential structure as other cells of the body. And thus the wonderful truth became manifest that a single cell may contain within its microscopic compass the sum-total of the heritage of the species. This conclusion first reached in the case of the female sex was soon afterward extended to the male as well. Since the time of Leeuwenhoek (1677) it had been known that the sperm or fertilizing fluid contained innumerable minute bodies endowed in nearly all cases with the power of active movement, and therefore regarded by the early observers as parasitic animalcules or infusoria, a view which gave rise to the name *spermatozoa* (sperm-animals) by which they are still generally known.[1] As long ago as 1786, however, it was shown by Spallanzani that the fertilizing power must lie in the spermatozoa, not in the liquid in which they swim, because the spermatic fluid loses its power when filtered. Two years after the appearance of Schwann's epoch-making work Kölliker demonstrated (1841) that the spermatozoa arise directly from cells in the testis, and hence cannot be regarded as parasites, but are, like the ovum, derived from the parent-body. Not until 1865, however, was the final proof attained by Schweigger-Seidel and La Valette St. George that the spermatozoön contains not only a nucleus, as Kölliker believed, but also cytoplasm. It was thus shown to be, like the egg, a single cell, peculiarly modified in structure, it is true, and of extraordinary minuteness, yet on the whole morphologically equivalent to other cells. A final step was taken ten years later (1875), when Oscar Hertwig established the all-important fact that fertilization of the egg is accomplished by its union with one spermatozoön, and one only. In sexual reproduction, therefore, each sex contributes a single cell of its own body to the formation of the offspring, a fact which beautifully tallies with the conclusion of Darwin and Galton that the sexes play, on the whole, equal, though not identical parts in hereditary transmission. The ultimate problems of sex, fertilization, inheritance, and development were thus shown to be *cell-problems*.

Meanwhile, during the years immediately following the announcement of the cell-theory, the attention of investigators was especially focussed upon the question: How do the cells of the body arise? The origin of cells by the division of preëxisting cells was clearly recognized by Hugo von Mohl in 1835, though the full significance of this epoch-making discovery was so obscured by the errrors of Schleiden and Schwann that its full significance was only perceived long afterward. The founders of the cell-theory were unfortunately led to the conclusion that cells might arise in two different ways, viz. either by division or fission of a preëxisting mother-cell, or by "free cell-formation," new cells arising in the latter case not from preexisting ones, but by crystallizing, as it were, out of a formative or nutritive substance, termed the "cytoblastema"; and they even believed the latter process to be the usual and typical one. It was only after many years of painstaking research that "free cell-formation" was absolutely proved to be a myth, though many of

---

[1] The discovery of the spermatozoa is generally accredited to Ludwig Hamm, a pupil of Leeuwenhoek (1677), though Hartsoeker afterward claimed the merit of having seen them as early as 1674 (Dr. Allen Thomson).

Schwann's immediate followers threw doubts upon it,[1] and as early as 1855 Virchow positively maintained the universality of cell-division, contending that every cell is the offspring of a preëxisting parent-cell, and summing up in the since famous aphorism, "*omnis cellula e cellula.*"[2] At the present day this conclusion rests upon a foundation so firm that we are justified in regarding it as a universal law of development.

Now, if the cells of the body always arise by the division of preexisting cells, all must be traceable back to the fertilized egg-cell as their common ancestor. Such is, in fact, the case in every plant and animal whose development is accurately known. The first step in development consists in the division of the egg into two parts, each of which is a cell, like the egg itself. The two then divide in turn to form four, eight, sixteen, and so on in more or less regular progression (Fig. 4.) until step by step the egg has split up into the multitude of cells which build the body of the embryo, and finally of the adult. This process, known as the *cleavage* or *segmentation* of the egg, was observed long before its meaning was understood. It seems to have been first definitely described in the case of the frog's egg, by Prévost and Dumas (1824), though earlier observers had seen it; but at this time neither the egg nor its descendants were known to be cells, and its true meaning was first clearly perceived by Bergmann, Kölliker, Reichert, Von Baer, and Remak, some twenty years later. The interpretation of cleavage as a process of cell-division was followed by the demonstration that cell-division does not begin with cleavage, but *can be traced back into the foregoing generation;* for the egg-cell, as well as the sperm-cell, arises by the division of a cell preexisting in the parent-body. *It is therefore derived by direct descent from an egg-cell of the foregoing generation, and so on ad infinitum.* Embryologists thus arrived at the conception so vividly set forth by Virchow in 1858[3] of an uninterrupted series of cell-divisions extending backward from existing plants and animals to that remote and unknown period when vital organization assumed its present form. Life is a continuous stream. The death of the individual involves no breach of continuity in the series of cell-divisions by which the life of the race flows onwards. The individual body dies, it is true, but the germ-cells live on, carrying with them, as it were, the traditions of the race from which they have sprung, and handing them on to their descendants.

---

[1] Among these may be especially mentioned Mohl, Unger, Nägeli, Martin Barry, Goodsir, and Remak.

[2] *Arch. für Path. Anat.*, VIII., p. 23, 1855.

[3] See the quotation from the original edition of the *Cellularpathologie* at the head of Chapter II., p. 63.

We have thus arrived at the form in which the problems of heredity and development confront the investigator of the present day. It remains to point out more clearly how they are related to the general problems of evolution and to those post-Darwinian discussions in which Weismann has taken so active a part. All theories of evolution take the facts of variation and heredity as fundamental postulates, for it is by variation that new characters arise and by heredity that they are perpetuated. Darwin recognized two kinds of variation, both of which, being inherited and maintained through the conserving action of natural selection, might give rise to a permanent transformation of species. The first of these includes congenital or inborn

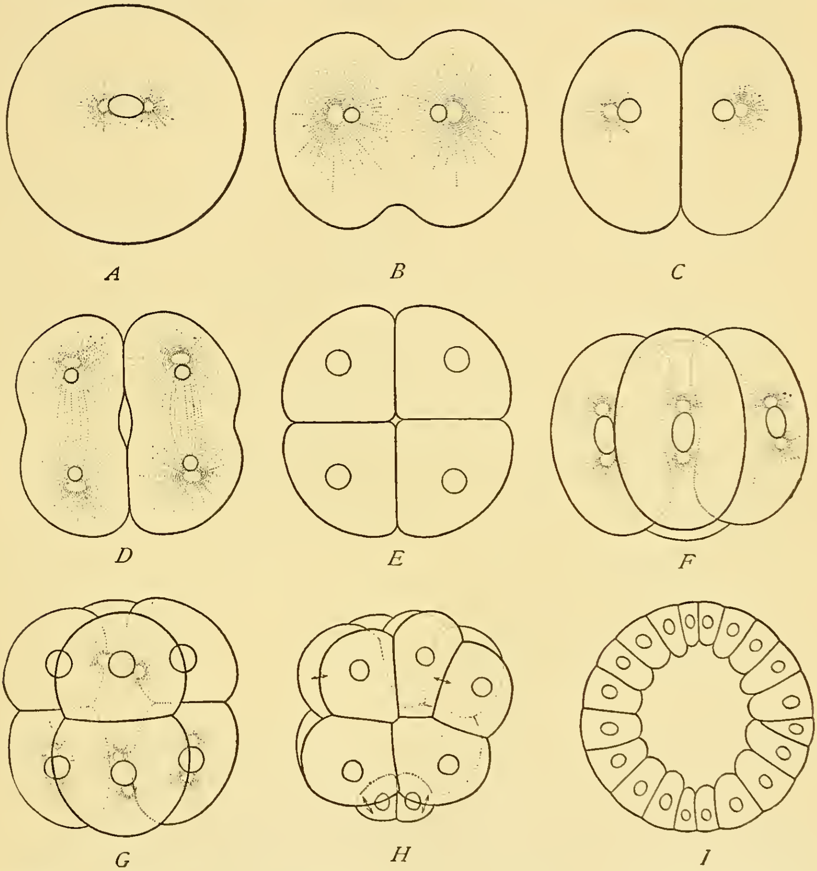

Fig. 4. — Cleavage of the ovum of the sea-urchin *Toxopneustes*, × 330, from life. The successive divisions up to the 16-cell stage (*H*) occupy about two hours. *I* is a section of the embryo (blastula) of three hours, consisting of approximately 128 cells surrounding a central cavity or blastocœl.

variations, *i.e.* such as appear at birth or are developed "spontaneously," without discoverable connection with the activities of the organism itself or the direct effect of the environment upon it, though Darwin clearly recognized the fact that even such variations must indirectly be due to changed conditions acting upon the parental organism or on the germ. In a second class of variations were placed the so-called acquired characters, *i.e.* definite effects directly produced in the course of the individual life as the result of use and disuse, or of food, climate, and the like. The inheritance of congenital characters is now universally admitted, but it is otherwise with acquired characters. The inheritance of the latter, now the most debated question of biology, had been taken for granted by Lamarck a half-century before Darwin; but he made no attempt to show how such transmission is possible. Darwin, on the other hand, squarely faced the physiological requirements of the problem, recognizing that the transmission of acquired characters can only be possible under the assumption that the germ-cell definitely reacts to all other cells of the body in such wise as to register the changes taking place in them. In his ingenious and carefully elaborated theory of pangenesis,[1] Darwin framed a provisional physiological hypothesis of inheritance in accordance with this assumption, suggesting that the germ-cells are reservoirs of minute germs or gemmules derived from every part of the body; and on this basis he endeavoured to explain the transmission both of acquired and of congenital variations, reviewing the facts of variation and inheritance with wonderful skill, and building up a theory which, although it forms the most speculative and hypothetical portion of his writings, must always be reckoned one of his most interesting contributions to science.

In the form advocated by Darwin the theory of pangenesis has been generally abandoned in spite of the ingenious attempt to remodel it made by Brooks in 1883.[2] In the same year the whole aspect of the problem was changed, and a new period of discussion inaugurated by Weismann, who put forth a bold challenge of the entire Lamarckian principle.[3] "I do not propose to treat of the whole problem of heredity, but only of a certain aspect of it, — the transmission of acquired characters, which has been hitherto assumed to occur. In taking this course I may say that it was impossible to avoid going back to the foundation of all phenomena of heredity, and to determine the substance with which they must be connected. In my opinion this can only be the substance of the germ-cells; and this substance transfers its hereditary tendencies from generation to generation, at first unchanged, and always uninfluenced in any corresponding manner, by that which happens during the life of the individual which bears it. If these views be correct, all our ideas upon the transformation of species require thorough modification, for the whole principle of evolution by means of exercise (use and disuse) as professed by Lamarck, and accepted in some cases by Darwin, entirely collapses" (*l.c.*, p. 69).

---

[1] *Variation of Animals and Plants,* Chapter XXVII.

[2] *The Law of Heredity,* Baltimore, 1883.

[3] *Ueber Vererbung,* 1883. See *Essays upon Heredity,* I., by A. Weismann, Clarendon Press, Oxford, 1889.

It is impossible, he continues, that acquired traits should be transmitted, for it is inconceivable that definite changes in the body, or "soma," should so affect the protoplasm of the germ-cells as to cause corresponding changes to appear in the offspring. How, he asks, can the increased dexterity and power in the hand of a trained piano-player so affect the molecular structure of the germ-cells as to produce a corresponding development in the hand of the child? It is a physiological impossibility. If we turn to the facts, we find, Weismann affirms, that not one of the asserted cases of transmission of acquired characters will stand the test of rigid scientific scrutiny. It is a reversal of the true point of view to regard inheritance as taking place from the body of the parent to that of the child. The child inherits from the parent *germ-cell*, not from the parent-body, and the germ-cell owes its characteristics not to the body which bears it, but to its descent from a preëxisting germ-cell of the same kind. Thus the body is, as it were, an offshoot from the germ-cell (Fig. 5). As far as inheritance is concerned, the body is merely the carrier of the germ-cells, which are held in trust for coming generations.

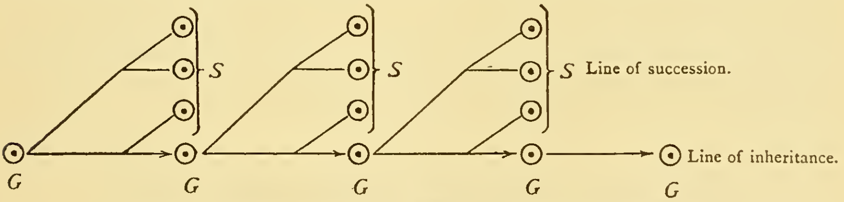

Fig. 5. — Diagram illustrating Weismann's theory of inheritance.

G. The germ-cell, which by division gives rise to the body or soma (*S*) and to new germ-cells (*G*) which separate from the soma and repeat the process in each successive generation.

Weismann's subsequent theories, built on this foundation, have given rise to the most eagerly contested controversies of the post-Darwinian period, and, whether they are to stand or fall, have played a most important part in the progress of science. For aside from the truth or error of his special theories, it has been Weismann's great service to place the keystone between the work of the evolutionists and that of the cytologists, and thus to bring the cell-theory and the evolution-theory into organic connection. It is from the point of view thus suggested that the present volume has been written. It has accordingly not been my primary object to dwell on the *minutiæ* of histology, still less to undertake an exhaustive description of all the modifications of cell-structure and cell-action; and for these the student must refer to other and more extended treatises. Yet the broader questions with which we have to deal cannot profitably be discussed apart from the concrete phenomena by which they are suggested, and hence a considerable part of the text is necessarily given over to descriptive detail; but I hope that the reader will not lose sight of the relation of the part to the whole, or forget the primary intention of the work.

We shall follow a convenient, rather than a strictly logical, order of treatment, beginning in the first two chapters with a general sketch of cell-structure and cell-division. The following three chapters deal with the germ-cells, — the third with their structure and mode of origin, the fourth with their union in fertilization, the fifth with the phenomena of maturation by which they are prepared for their union. The sixth chapter contains a critical discussion of cell-organization, completing the morphological analysis of the cell. In the seventh chapter the cell is considered with reference to its more fundamental chemical and physiological properties as a prelude to the examination of development which follows. The succeeding chapter approaches the objective point of the book by considering the cleavage of the ovum and the general laws of cell-division of which it is an expression. The ninth chapter, finally, deals with the elementary operations of development considered as cell-functions and with the theories of inheritance and development based upon them.

SOME GENERAL WORKS ON THE CELL-THEORY[1]

Bergh, R. S. — Vorlesungen über die Zelle und die einfachen Gewebe: *Wiesbaden*, 1894.

Carnoy, J. B. — La Biologie Cellulaire: *Lierre*, 1884.

Delage, Yves. — La Structure du Protoplasma et les Théories sur l'Hérédité et les grands Problèmes de la Biologie Générale: *Paris*, 1895.

Geddes & Thompson. — The Evolution of Sex: *New York*, 1890.

Häcker, V. — Praxis und Theorie der Zellen- und Befruchtungslehre: *Jena*, 1899.

Henneguy, L. F. — Leçons sur la Cellule: *Paris*, 1896.

Hertwig, O. — Die Zelle und die Gewebe: *Fischer, Jena*, I., 1893, II., 1898. Translation, published by *Macmillan, London and New York*, 1895.

Hofmeister. Lehre von der Pflanzenzelle: *Leipzig*, 1867.

Huxley, T. H. — Review of the Cell-theory: *British and Foreign Medico-Chirurgical Review*, XII., 1853.

---

[1] See also Literature, I., p. 61.

Minot, C. S. — Human Embryology: *New York*, 1892.

Remak, R. — Untersuchungen über die Entwicklung der Wirbelthiere: *Berlin*, 1850–55.

Sachs, J. v. History of Botany. Translation: *Oxford*, 1890.

Schleiden, M. J. — Beiträge zur Phytogenesis: *Müller's Archiv*, 1838. Translation in Sydenham Soc., XII. *London*, 1847.

Schwann, Th. — Mikroscopische Untersuchungen über die Uebereinstimmung in der Structur und dem Wachsthum der Thiere und Pflanzen: *Berlin*, 1839. Translation in Sydenham Soc., XII. *London*, 1847.

Tyson, James. — The Cell-doctrine, 2d ed. *Philadelphia*, 1878.

Virchow, R. — Die Cellularpathologie in ihrer Begründung auf physiologische und pathologische Gewebelehre: *Berlin*, 1858.

Weismann, A. — Essays on Heredity. Translation: First series, *Oxford*, 1891; Second series, *Oxford*, 1892.

Id. — The Germ-plasm: *New York*, 1893.

CHAPTER I

GENERAL SKETCH OF THE CELL

> "Wir haben gesehen, dass alle Organismen aus wesentlich gleichen Theilen, nämlich aus Zellen zusammengesetzt sind, dass diese Zellen nach wesentlich denselben Gesetzen sich bilden und wachsen, dass also diese Prozesse überall auch durch dieselben Kräfte hervorgebracht werden müssen."
>
> SCHWANN.[1]

In the passage quoted above Schwann expressed a truth which subsequent research has established on an ever widening basis; and we have now more than ever reason to believe that despite unending diversity of form and function all cells may be brought into definite relation to a common morphological and physiological type. We are, it is true, still unable to specify all its essential features, and hence can give no adequate brief definition of the cell. For practical purposes, however, no such definition is needed, and we may be content with the simple type that has been familiar to histologists since the time of Leydig and Max Schultze.

It should from the outset be clearly recognized that the term "cell" is a biological misnomer; for cells only rarely assume the form implied by the word of hollow chambers surrounded by solid walls. The term is merely an historical survival of a word casually employed by the botanists of the seventeenth century to designate the cells of certain plant-tissues which, when viewed in section, give somewhat the appearance of a honeycomb.[2] The cells of these tissues are, in fact, separated by conspicuous solid walls which were mistaken by Schleiden, followed by Schwann, for their essential part. The living substance contained within the walls, to which Hugo von Mohl gave the name *protoplasm*[3] (1846), was at first overlooked or was regarded as a waste-product, a view based upon the fact that in many important plant-tissues such as cork or wood it may wholly disappear, leaving only the lifeless walls. The researches of Bergmann, Kölliker, Bischoff, Cohn, Max Schultze, and many others showed, however, that most living cells are not hollow but solid bodies, and that in many cases — for example, the colourless corpuscles of blood and lymph — they are naked masses of protoplasm not surrounded by definite walls. Thus it was proved that neither the vesicular form nor the presence of surrounding walls is an essential character, and that the cell-contents, *i.e.* the *protoplasm*, must be the seat of vital activity.

---

[1] *Untersuchungen*, p. 227, 1839.

[2] The word seems to have been first employed by Robert Hooke, in 1665, to designate the minute cavities observed in cork, a tissue which he described as made up of "little boxes or cells distinct from one another" and separated by solid walls.

[3] The same word had been used by Purkinje some years before (1840) to designate the formative material of young animal embryos.

Within the protoplasm (Figs. 6–8) lies a body, usually of definite rounded form, known as the *nucleus*,[1] and this in turn often contains one or more smaller bodies or *nucleoli*. By some of the earlier workers the nucleus was supposed to be, like the cell-wall, of secondary importance, and many forms of cells were described as being devoid of a nucleus ("cytodes" of Haeckel). Nearly all later researches have indicated, however, that the characteristic nuclear material, whether forming a single body or scattered in smaller masses, is always present, and that it plays an essential part in the life of the cell.

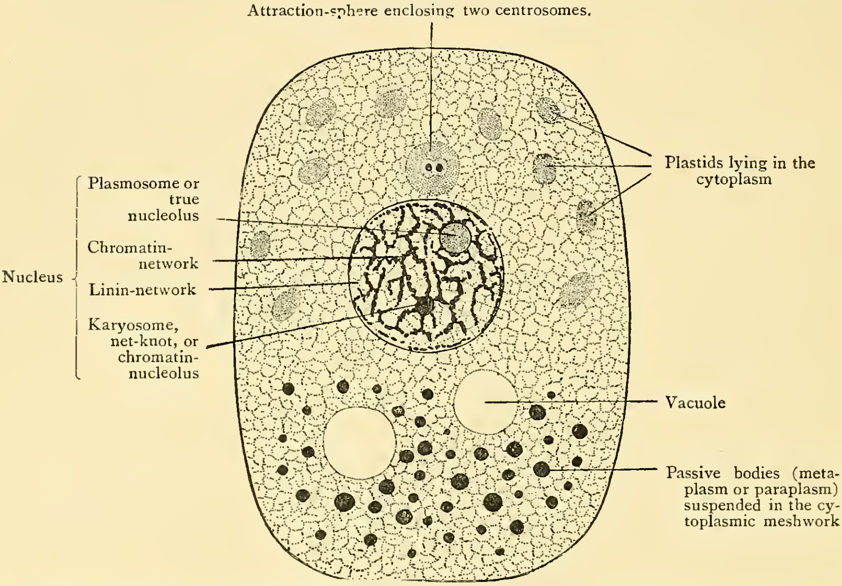
Attraction-sphere enclosing two centrosomes.
Plastids lying in the cytoplasm
Nucleus
Plasmosome or true nucleolus
Chromatin-network
Linin-network
Karyosome, net-knot, or chromatin-nucleolus
Vacuole
Passive bodies (metaplasm or paraplasm) suspended in the cytoplasmic meshwork

Fig. 6. — Diagram of a cell. Its basis consists of a meshwork containing numerous minute granules (*microsomes*) and traversing a transparent ground-substance.

Besides the presence of protoplasm and nucleus, no other structural features of the cell are yet known to be of universal occurrence.

---

[1] First described by Fontana in 1781, and recognized as a normal element of the cell by Robert Brown in 1833.

We may therefore still accept as valid the definition given more than thirty years ago by Leydig and Max Schultze, that a cell is *a mass of protoplasm containing a nucleus*,[1] to which we may add Schultze's statement that *both nucleus and protoplasm arise through the division of the corresponding elements of a preëxisting cell.* Nothing could be less appropriate than to call such a body a "cell"; yet the word has become so firmly established that every effort to replace it by a better has failed, and it probably must be accepted as part of the established nomenclature of science.[2]

A. General Morphology of the Cell

The cell is a rounded mass of protoplasm which in its simplest form is approximately spherical. The form is, however, seldom realized save in isolated cells such as the unicellular plants and animals or the egg-cells of the higher forms. In vastly the greater number of cases the typical spherical form is modified by unequal growth and differentiation, by active movements of the cell-substance, or by the mechanical pressure of surrounding structures, but true angular forms are rarely if ever assumed save by cells surrounded by hard walls. The protoplasm which forms its active basis is a viscid, translucent substance, sometimes apparently homogeneous, more frequently finely granular, and as a rule giving the appearance of a meshwork, which is often described as a spongelike or netlike "reticulum."[3] Besides the active substance or protoplasm proper the cell almost invariably contains various lifeless bodies suspended in the meshes of the network; examples of these are food-granules, pigment-bodies, drops of oil or water, and excretory matters. These bodies play a relatively passive part in the activities of the cell, being either reserve food-matters destined to be absorbed and built up into the living substance, or by-products formed from the protoplasm as waste-matters or in order to play some *rôle* subsidiary to the actions of the protoplasm itself. The passive inclusions in the protoplasm may be collectively designated as *metaplasm* (Hanstein) or *paraplasm* (Kupffer), in contradistinction to the active *protoplasm.*

---

[1] Leydig, *Lehrbuch der Histologie*, p. 9, 1857; Schultze, *Arch. Anat. u. Phys.*, p. 11, 1861.

[2] Sachs has proposed the convenient word *energid* (*Flora*, '92, p. 57) to designate the essential living part of the cell, *i.e.* the nucleus with that portion of the active cytoplasm that falls within its sphere of influence, the two forming an organic unit both in a morphological and in a physiological sense. It is to be regretted that this convenient and appropriate term has not come into general use. (See also *Flora*, '95, p. 405, and *cf.* Kupffer ('96), Meyer ('96), and Kölliker ('97).)

[3] Such meshworks are sometimes plainly visible in the living protoplasm (p. 44). It is always more or less an open question how far the appearances seen in fixed (coagulated) material correspond with the conditions existing in life. See pp. 42–46.

It is often difficult to distinguish between such metaplasmic bodies and the granules commonly supposed to be elements of the active protoplasm; indeed, as will appear beyond (p. 29), there is reason to believe that "protoplasmic" and "metaplasmic" granules cannot be separated by any definite limit, but are connected by various gradations. Among the lifeless products of the protoplasm must be reckoned also the *cell-wall* or *membrane* by which the cell-body may be surrounded; but it must be remembered that the cell-wall in some cases arises by a direct transformation of the protoplasmic substance, and that it often retains the power of growth by intussusception like living matter.

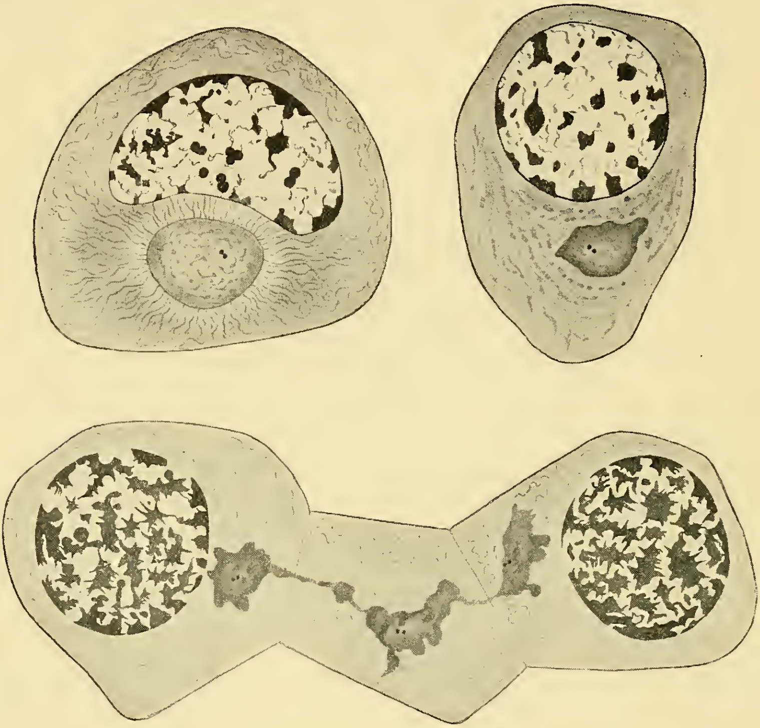

Fig. 7 — Spermatogonia of the salamander. [MEVES.]

Above, two cells showing large nuclei, with linin-threads and scattered chromatin-granules; in each cell an attraction-sphere with two centrosomes. Below, three contiguous spermatogonia, showing chromatin-reticulum, centrosomes and spheres, and sphere-bridges.

It is unfortunate that some confusion has arisen in the use of the word *protoplasm*. When Leydig, Schultze, Brücke, De Bary, and other earlier writers spoke of "protoplasm," they had in mind only the substance of the cell-body, not that of the nucleus. Strasburger, however, in 1882, extended the term so as to denote the entire active cell-substance, including the nuclear material, suggesting that the latter be called *nucleoplasm*, and that of the cell-body *cytoplasm.*

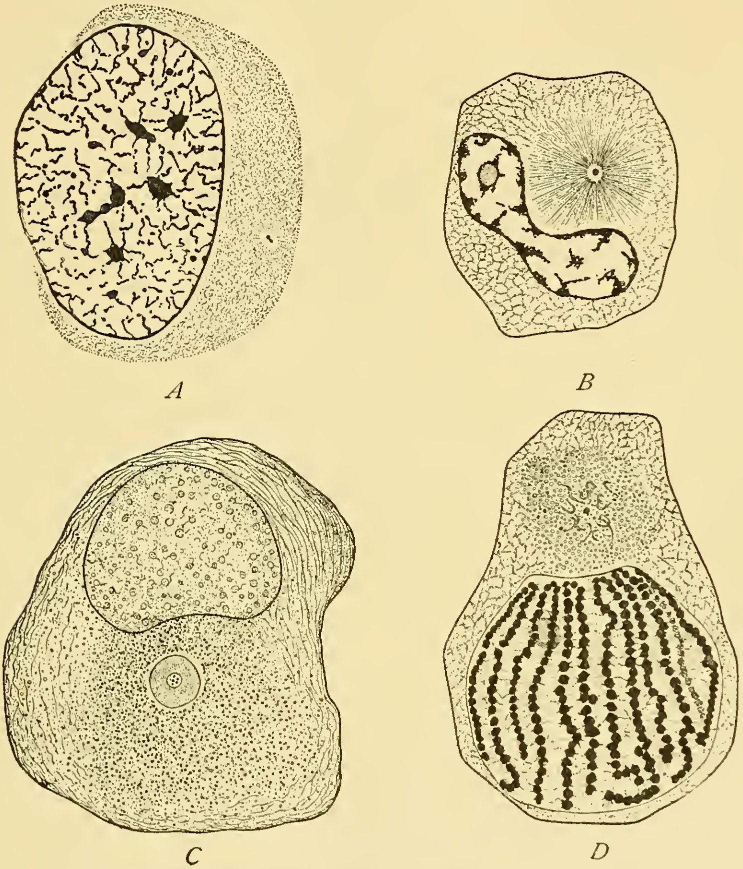

Fig. 8 — Various cells showing the typical parts.

A. From peritoneal epithelium of the salamander-larva. Two centrosomes at the right Nucleus showing net-knots. [FLEMMING.]

B. Spermatogonium of frog. Attraction-sphere (aster) containing a single centrosome Nucleus with a single plasmosome. [HERMANN.]

C. Spinal ganglion-cell of frog. Attraction-sphere near the centre, containing a single centrosome with several centrioles. [LENHOSSÉK.]

D. Spermatocyte of *Proteus.* Nucleus in the spireme-stage. Centrosome single; attraction-sphere containing rod-shaped bodies. [HERMANN.]

These terms have been adopted by many, but not all, later writers, the hybrid word *nucleoplasm* having, however, at Flemming's suggestion, been changed to *karyoplasm.* At the present time, therefore, the word *protoplasm* is used by some authors (Bütschli, Hertwig, Kölliker, etc.) in its original narrower sense (equivalent to Strasburger's *cytoplasm*), while perhaps the majority of writers have accepted the terminology of Strasburger and Flemming. On the whole, the terms *cytoplasm* and *karyoplasm* seem too useful to be rejected, and, without attaching too much importance to them, they will be employed throughout the present work. It must not, however, be supposed that either of the words denotes a single homogeneous substance; for, as will soon appear, both cytoplasm and karyoplasm consist of several distinct elements.

The nucleus is usually bounded by a definite membrane, and often appears to be a perfectly distinct vesicular body suspended in the cytoplasm — a conclusion sustained by the fact that it may move actively through the latter, as often occurs in both vegetable and animal cells. Careful study of the nucleus during all its phases gives, however, reason to believe that its structural basis is similar to that of the cell-body; and that during the course of cell-division, when the nuclear membrane usually disappears, cytoplasm and karyoplasm come into direct continuity. Even in the resting cell there is good evidence that both the intranuclear and the extranuclear material may be structurally continuous with the nuclear membrane[1] and among the Protozoa there are forms (some of the flagellates) in which no nuclear membrane can at any period be seen. For these and other reasons *the terms "nucleus" and "cell-body" should probably be regarded as only topographical expressions denoting two differentiated areas in a common structural basis.* The terms *karyoplasm* and *cytoplasm* possess, however, a specific significance owing to the fact that there is on the whole a definite chemical contrast between the nuclear substance and that of the cell-body, the former being characterized by the abundance of a substance rich in phosphorus known as *nuclein*, while the latter contains no true nuclein and is especially rich in albuminous substances such as nucleo-albumins, albumins, globulins, and the like, which contain little or no phosphorus.

Both morphologically and physiologically the differentiation of the active cell-substance into nucleus and cell-body must be regarded as a fundamental character of the cell because of its universal, or all but universal, occurrence, and because there is reason to believe that it is in some manner an expression of the dual aspect of the fundamental process of metabolism, constructive and destructive, that lies at the basis of cell life. The view has been widely held that a third essential element is the *centrosome*, discovered by Flemming and Van Beneden in 1875–76, and since shown to exist in a large number of other cells (Figs. 7, 8). This is an extremely minute body which is concerned in the process of cell-division and in the fertilization of the egg, and has been characterized as the "dynamic centre" of the cell. Whether it has such a significance, and whether it is in point of morphological persistence comparable with the nucleus, are questions still *sub judice*, which will be discussed elsewhere.[1]

---

[1] Conklin ('97, 1), Obst ('99), and some others have described a direct continuity in the resting cell between the intranuclear and extranuclear meshworks.

B. STRUCTURAL BASIS OF PROTOPLASM

As ordinarily seen under moderate powers of the microscope, protoplasm appears as a more or less vague granular substance which shows as a rule no definite structure organization. More precise examination under high powers, especially after treatment by suitable fixing and staining reagents, often reveals a highly complex structure in both nucleus and cytoplasm. Since the fundamental activities of protoplasm are everywhere of the same nature, investigators have naturally sought to discover a corresponding fundamental morphological organization common to all forms of protoplasm and underlying all of its special modifications. Up to the present time, however, these attempts have not resulted in any *consensus* of opinion as to whether such a common organization exists. In many forms of protoplasm, both in life and after fixation by reagents, the basis of the structure is a more or less regular framework or *meshwork*, consisting of at least two substances. One of these forms the substance of the meshwork proper; the other, often called the *ground-substance* (also cell-sap, enchylema, hyaloplasma, paramitome, interfilar substance, etc.),[2] occupies the intervening spaces. To these two elements must be added minute, deeply staining *granules* or "microsomes" scattered along the branches of the meshwork, sometimes quite irregularly, sometimes with such regularity that the meshwork seems to be built of them. Besides the foregoing three elements, which we may provisionally regard as constituting the active substance, the protoplasm almost invariably contains various passive or metaplasmic substances in the form of larger granules, drops of liquid, crystalloid bodies, and the like. These bodies, which usually lie in the spaces of the meshwork, are often difficult to distinguish from the microsomes lying in the meshwork proper — indeed, it is by no means certain that any adequate ground of distinction exists.[3]

From the time of Frommann and Arnold ('65–'67) onwards, most of the earlier observers regarded the meshwork as a fibrillar structure, either forming a continuous network or *reticulum* somewhat like the fibrous network of a sponge ("reticular theory" of Klein, Van Beneden, Carnoy, Heitzmann), or consisting of disconnected threads,

---

[1] *Cf.* pp. 304, 354.

[2] *Cf.* Glossary.

[3] *Cf.* p. 29.

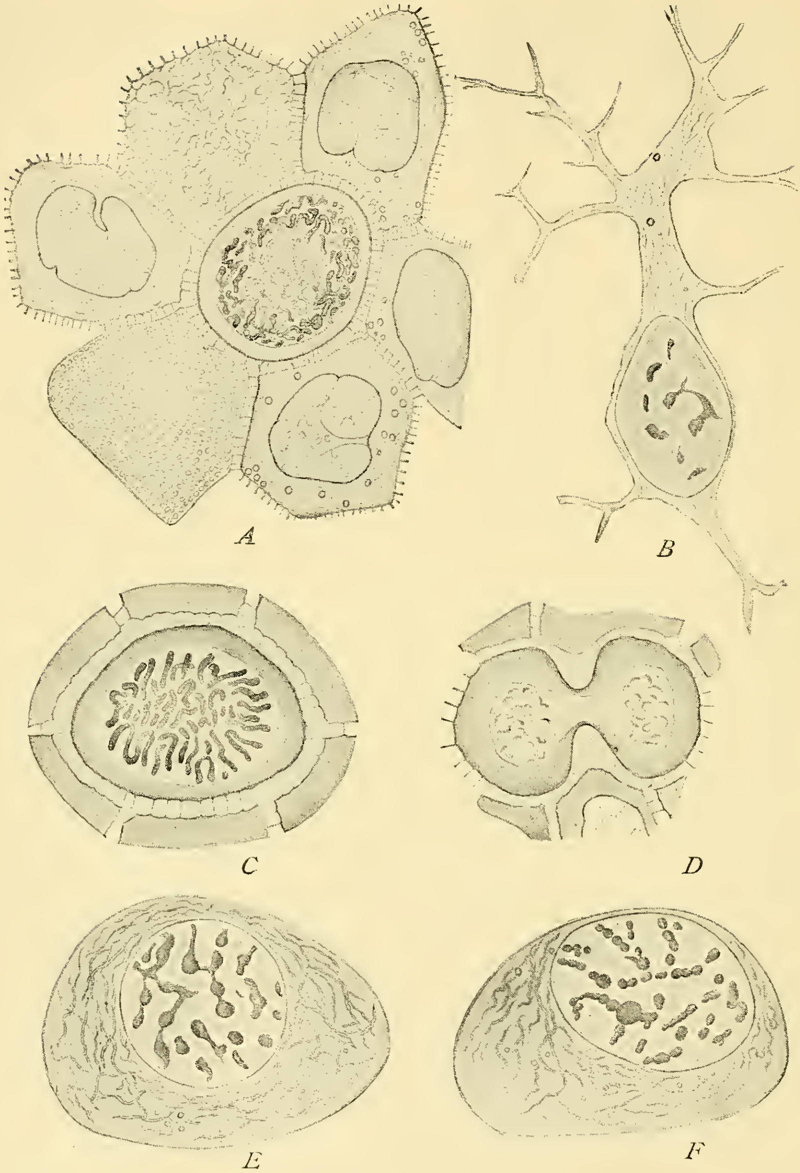

Fig. 9. — Living cells of salamander-larva. [FLEMMING.]

A. Group of epidermal cells at different foci, showing protoplasmic bridges, nuclei, and cytoplasmic fibrillæ; the central cell with nucleus in the spireme-stage. *B.* Connective tissue cell. *C.* Epidermal cell in early mitosis (segmented spireme) surrounded by protoplasmic bridges. *D.* Dividing cell. *E.F.* Cartilage-cells with cytoplasmic fibrillæ (the latter somewhat exaggerated in the plate).

whether simple or branching ("filar theory" of Flemming), and the same view is widely held at the present time. The meshwork has received various names in accordance with this conception, among which may be mentioned *reticulum*, *thread-work*, *spongioplasm*, *mitome*, *filar substance*,[1] all of which are still in use. Under this view the "granules" described by Schultze, Virchow and still earlier observers have been variously regarded as nodes of the network, optical sections of the threads, or as actual granules ("microsomes") suspended in the network as described above.

Widely opposed to these views is the "alveolar theory" of Bütschli, which has won an increasing number of adherents. Bütschli regards protoplasm as having a foam-like alveolar structure ("Wabenstruktur"), nearly similar to that of an emulsion (Fig. 10), and he has shown in a series of beautiful experiments that artificial emulsions, variously prepared, may show under the microscope a marvellously close resemblance to living protoplasm, and further that drops of oil-emulsion suspended in water may even exhibit amœboid changes of form. To restate Bütschli's view, protoplasm consists of separate, closely crowded minute drops[2] of a liquid *alveolar substance* suspended in a continuous *interalveolar substance*, likewise liquid, but of different physical nature. The latter thus forms the walls of closed chambers or *alveoli* in which the alveolar drops lie, just as in a fine emulsion the emulsifying liquid surrounds the emulsified drops. The appearance of a network in protoplasm is illusory, being due to optical section of the interalveolar walls or partitions as viewed at any given focus of the microscope. As thus seen, the walls themselves appear as fibres, while the "spaces of the network" are in like manner optical sections of the alveoli, the alveolar substance that fills them corresponding to the "ground substance." As explained beyond,[3] Bütschli interprets in like manner the radiating systems or asters formed during cell-divison, the astral rays (usually considered as fibres) being regarded as merely the septa between radially arranged alveoli (Fig. 10).

The two (three) general views above outlined may be designated respectively as the *fibrillar* (reticular or filar) and *alveolar* theories of protoplasmic structure; and each of them has been believed by some of its adherents to be universally applicable to all forms of protoplasm. Beside them may be placed, as a third general view, the *granular* theory especially associated with the name of Altmann, by whom it has been most fully developed, though a number of earlier writers have held similar views. According to Altmann's view, which apart from its theoretical development approaches in some respects that of Bütschli, protoplasm is compounded of innumerable minute granules which alone form its essential active basis; and while fibrillar or alveolar structures may occur, these are of only secondary importance.

---

[1] See Glossary.

[2] Measuring on an average about .001 mm. in diameter.

[3] *Cf.* p. 110.

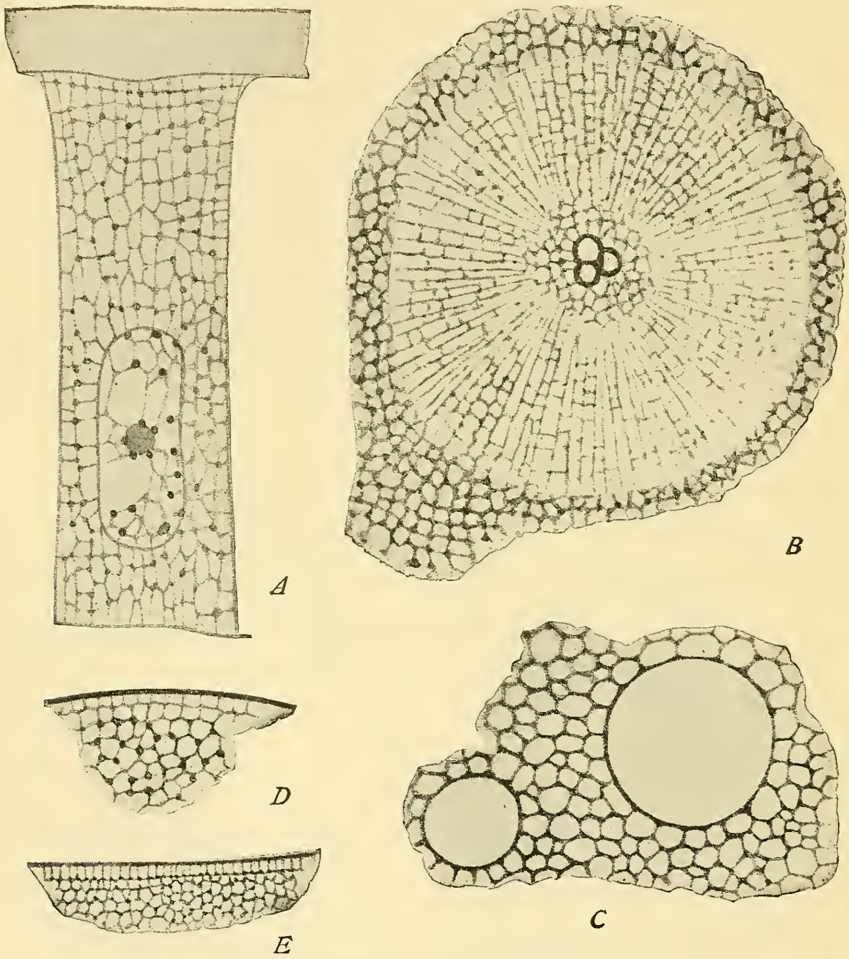

Fig. 10. — Alveolar or foam-structure of protoplasm, according to Bütschli. [BÜTSCHLI.]

A. Epidermal cell of the earthworm. *B.* Aster, attraction-sphere, and centrosome from sea-urchin egg. *C.* Intracapsular protoplasm of a radiolarian (*Thalassicolla*) with vacuoles. *D.* Peripheral cytoplasm of sea-urchin egg. *E.* Artificial emulsion of olive-oil, sodium chloride, and water.

It is impossible here adequately to review the many combinations and modifications of these views which different investigators have made.[1] On the whole, the present drift of opinion is toward the conclusion that none of the above interpretations has succeeded in the attempt to give a universal formula for protoplasmic structure; and many recent observers have reached the conclusion, earlier advocated by Kölliker ('89), that the various types described above are connected by intermediate gradations and may be transformed one into another, in different phases of cell-activity. Unna ('95), for example, endeavours to show how an alveolar structure may pass into a sponge-like or reticular one by the breaking down of the inter-alveolar walls. Flemming, for many years the foremost and most consistent advocate of the fibrillar theory, now admits that protoplasm may be fibrillar, alveolar, granular, or sensibly homogeneous,[2] and that we cannot, therefore, regard any one of these types of structure as absolutely diagnostic of the living substance. In plant-cells Strasburger[3] and a number of his pupils maintain that the "kinoplasm" (p. 322) or filar plasm, from which the spindle-fibres and astral rays are formed, is fibrillar, while the "trophoplasm" or alveolar plasm forming the main body of the cell is alveolar, the former, however, assuming the fibrillar structure, as a rule, only during the mitotic activity of the cell. My own long-continued studies on various forms of protoplasm have likewise led to the conclusion that no universal formula for protoplasmic structure can be

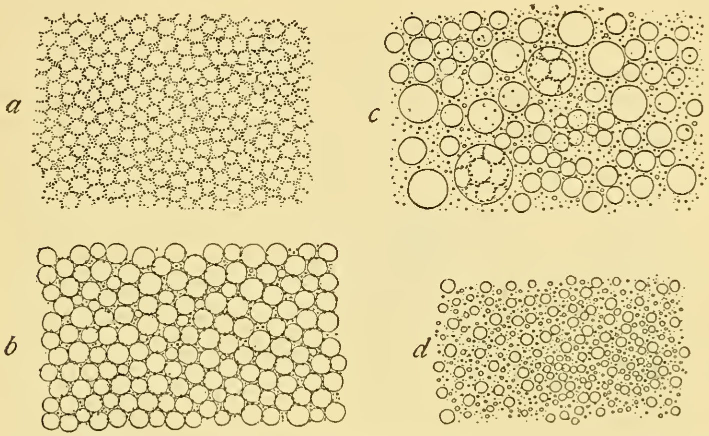

Fig. 11. — (*a*) Protoplasm of the egg of the sea-urchin (*Toxopneustes*) in section showing meshwork of microsomes; (*b*) protoplasm from a living star-fish egg (*Asterias*) showing alveolar spheres with microsomes scattered between them; (*c*) the same in a dying condition after crushing the egg; alveolar spheres fusing to form larger spheres; (*d*) protoplasm from a young ovarian egg of the same. (All the figures magnified 1200 diameters.)

---

[1] For full discussion, with literature list, see Flemming, '82, '97, 1, '97, 2, and Bütschli, '92, 2, '99.

[2] '97, 1, p. 260.

[3] '95, '97, 3, '98.

given.[1] In that classical object, the echinoderm-egg, for example, it is easy to satisfy oneself, *both in the living cell and in sections*, that the protoplasm has a beautiful alveolar structure, exactly as described by Bütschli in the same object (Fig. 11). This structure is here, however, entirely of secondary origin; for its genesis can be traced step by step during the growth of the ovarian eggs through the deposit of minute drops in a homogeneous basis, which ultimately gives rise to the interalveolar walls. In these same eggs the astral systems formed during their subsequent division (Fig. 12) are, I believe, no less certainly fibrillar; and thus we see the protoplasm of the same cell passing successively through homogeneous, alveolar, and fibrillar phases, at different periods of growth and in different conditions of physiological activity. There is good reason to regard this as typical of protoplasm in general. Bütschli's conclusions, based on researches so thorough, prolonged, and ingenious, are entitled to great weight; yet it is impossible to resist the evidence that fibrillar and granular as well as alveolar structures are of wide occurrence; and while each may be characteristic of certain kinds of

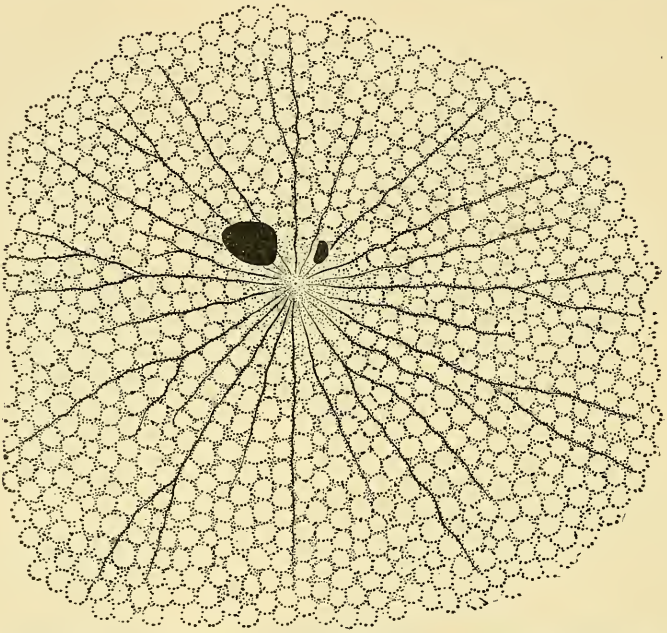

Fig. 12.—Section of sea-urchin egg (*Toxopneustes*), 1½ minutes after entrance of the spermatozoön, showing alveoli and microsomes, sperm-nucleus, middle piece, and aster (about 2000 diameters).

---

[1] Wilson, '99.

cells, or of certain physiological conditions,[1] none is common to all forms of protoplasm. If this position be well grounded, we must admit that the attempt to find in visible protoplasmic structure any adequate insight into its fundamental modes of physiological activity has thus far proved fruitless. We must rather seek the source of these activities in the ultramicroscopical organization, accepting the probability that apparently homogeneous protoplasm is a complex mixture of substances which may assume various forms of visible structure according to its modes of activity.

Some of the theoretical speculations regarding the essential nature of that organization are discussed in Chapter VI., but one *quasi*-theoretical point must be here considered. Much discussion has been given to the question as to which of the visible elements of the protoplasm should be regarded as the "living" substance proper; and the diversity of opinion on this subject may be judged by the fact that although many of the earlier observers identified the "reticulum" as the living element, and the ground-substance as lifeless, others, such as Leydig and Schäfer, held exactly the reverse view, while Altmann insisted that only the "granules" were alive. Later discussions have shown the futility of this discussion, which is indeed largely a verbal one, turning as it does on the sense of the word "living." In practice we continually use the word "living" to denote various degrees of vital activity. Protoplasm deprived of nuclear matter has lost, wholly or in part, one of the most characteristic vital properties, namely, the power of synthetic metabolism; yet we still speak of it as "living," since it still retains for a longer or shorter period such properties as irritability and the power of coördinated movement; and, in like manner, various special elements of protoplasm may be termed "living" in a still more restricted sense. In its fullest meaning, however, the word "living" implies the existence of a group of coöperating activities more complex than those manifested by any one substance or structural element. I am therefore entirely in accord with the view urged by Sachs, Kölliker, Verworn, and other recent writers, that life can only be properly regarded as a property of the cell-system as a whole; and the separate elements of the system would, with Sachs, better be designated as "active" or "passive," rather than as "living" or "lifeless." Thus regarded, the distinction between "protoplasmic" and "metaplasmic" substances, while a real and necessary one, becomes after all one of degree. I believe that we are probably justified in regarding the continuous substance as the most constant and active element, and that which forms the fundamental basis of the system, transforming itself into granules, drops, fibrillæ, or networks in accordance with varying physiological needs.[1]

---

[1] Thus the alveolar structure seems to be characteristic of Protozoa in general, and of the protoplasm of plant-cells when in the vegetative state, the fibrillar of nerve-cells and muscle-cells. The granular type is characteristic of some forms of leucocytes and gland-cells; but many of the granules in these cells are no doubt metaplasmic, and it is further very doubtful whether such a granular or "pseudo-alveolar" structure can be logically distinguished from an alveolar (*cf.* Wilson, '99). In the pancreas-cell granular and fibrillar structures alternate with the varying phases of secretory activity (*cf.* Mathews, '99).

Thus stated, the question as to the relative activity of the various elements becomes a real and important one. It now seems probable that the substance of the meshwork (fibrillar or interalveolar structure) is most active in the processes of cell-division, in contractile organs such as cilia and muscle-fibres, and in nerve-cells; but the ground-substance, while apparently the most frequent seat of metaplasmic deposits, is certainly also the seat of active chemical changes. This subject has, however, not yet been sufficiently investigated.

C. The Nucleus

A fragment of a cell deprived of its nucleus may live for a considerable time and manifest the power of coördinated movement without perceptible impairment. Such a mass of protoplasm is, however, devoid of the powers of assimilation, growth, and repair, and sooner or later dies. In other words, those functions that involve destructive metabolism may continue for a time in the absence of the nucleus; those that involve constructive metabolism cease with its removal. There is, therefore, strong reason to believe that the nucleus plays an essential part in the constructive metabolism of the cell, and through this is especially concerned with the formative processes involved in growth and development. For these and many other reasons, to be discussed hereafter, the nucleus is generally regarded as a controlling centre of cell-activity, and hence a primary factor in growth, development, and the transmission of specific qualities from cell to cell, and so from one generation to another.

---

[1] Wilson, '99. *Cf.* Sachs ('92, '95), Kölliker ('97), Meyer ('96), and Kupffer ('96) on energids. Sachs sharply distinguishes between the *energid* (nucleus and protoplasm), which forms a living unit, and the passive energid-*products*, placing in the former the nucleus, nucleolus, general cytoplasm, centrosome and plastids (chloroplasts and leucoplasts), and in the latter the starch-grains, aleurone-crystals, and membrane. Meyer carries the analysis further, classifying the active energid-elements into *protoplasmatic* and *alloplasmatic* organs, the former (nucleus cytoplasm, chromatophores, and perhaps the centrosomes) arising only by division, the latter (cilia, and according to Kölliker, also the muscle- and nerve-fibrillæ) formed by differentiation from the protoplasmatic elements. The passive energid-products (*ergastic* structures or "formed material" of Beale) are formed as *enclosures* (starch-grains, etc.), or excretions (membranes). These general views are accepted by Kölliker; but none of these writers has undertaken to show how "alloplasmatic" structures are to be distinguished from metaplasmic or ergastic. I believe Sachs' view to be in principle not only true but of high utility. Practically, however, it involves us in considerable difficulty, unless the terminology adopted above — itself directly suggested by and nearly agreeing with the usage of Sachs and Kölliker — be employed.

1. *General Structure*

The cell-nucleus passes through two widely different phases, one of which is characteristic of cells in their ordinary or vegetative condition, while the other only occurs during the complicated changes involved in cell-division. In the first phase, falsely characterized as the "resting state," the nucleus usually appears as a rounded sac-like body surrounded by a distinct membrane and containing a conspicuous irregular network (Figs. 6, 7, 13), which is in some cases plainly visible in the living cell (Fig. 9). The form of the nucleus, though subject to variation, is on the whole singularly constant, and as a rule shows no very definite relation to that of the cell-body, though in elongated cells such as muscle-cells, in certain forms of parenchyma, and in epithelial cells (Fig. 49), the nucleus is itself often elongated. Typically spherical, it may, in certain cases, assume an irregular or amœboid form, may break up into a group of more or less completely separated lobes (polymorphic nuclei, Fig. 49), sometimes forming an irregular ring ("ring-nuclei" of leucocytes, giant-cells, etc., Fig. 14, *D*). It is usually very large in gland-cells and others that show a very active metabolism, and in such cases its surface is sometimes increased by the formation of complex branches ramifying through the cell (Fig. 14, *E*).

These forms seem in general to be fairly constant in a given species of cell, but in a large number of cases the nucleus has been seen in the living cell (cartilage-cells, leucocytes, ova) to undergo more or less active changes of form, sometimes so marked as to merit the name of amœboid (Fig. 77). Perhaps the most remarkable deviations from the usual type of nucleus occur among the unicellular forms. In the ciliate Infusoria the nuclei are massive bodies of two kinds, viz. a large *macronucleus* and one or more smaller *micronuclei*, both of which are present in the same cell, the former kind being generally regarded as the active nucleus, the latter as a reserve nucleus from which at certain periods new macronuclei arise (p. 224). The macronuclei show a remarkable diversity of form and structure in different species. Still more interesting are the so-called scattered or distributed nuclei, described by Bütschli in flagellates and Bacteria, by Gruber in certain rhizopods and Infusoria, and by several authors in the Cyanophyceæ (Figs. 15, 16). The nuclear material is here apparently scattered through the cell in the form of numerous minute, deeply stained granules, which, if this identification is correct, represent the most primitive known types of nucleus; but this subject is still *sub judice* (p. 39). A transition from this condition to nuclei of the ordinary type appears to be given in the nuclei of certain flagellates (e.g. *Chilomonas* and *Trachelmonas*), where the chromatin-granules are aggregated about a nucleolus-like body, but are not enclosed by a membrane.[1]

In considering the structure of the nucleus, as seen in sections, we must, as in the case of the cytoplasm, bear in mind the possibility, or rather probability, that some of the elements described may be coagulation-products; for the nucleus is in life composed of liquid or semi-liquid substance, and Albrecht ('99) has recently shown that nuclei isolated in the fresh condition will flow together to form a single body. Most of the main features of the nucleus, both in the resting and in the dividing phases, have, however, been seen in life (Fig. 9), and the principal danger of mistaking artifacts for normal structures relates to the finer elements, considered beyond.

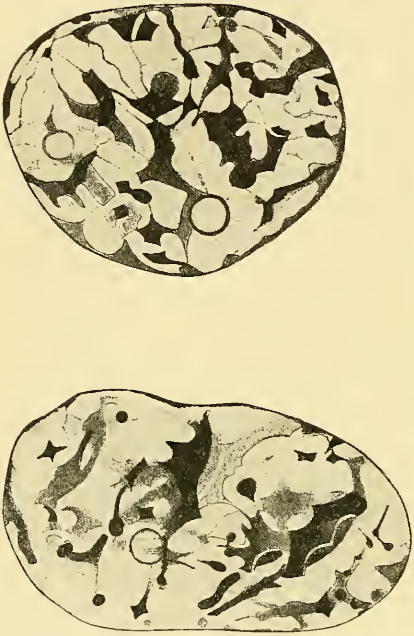

Fig. 13. — Two nuclei from the crypts of Lieberkühn in the salamander. [HEIDENHAIN.]

The character of the chromatin-network (*basichromatin*) is accurately shown. The upper nucleus contains three plasmosomes or true nucleoli; the lower, one. A few fine linin-threads (*oxychromatin*) are seen in the upper nucleus running off from the chromatin-masses. The clear spaces are occupied by the ground-substance.

In the ordinary forms of nuclei in their resting state the following structural elements may as a rule be distinguished (Figs. 6, 7, 10): —

a. The *nuclear membrane*, a well-defined delicate wall which gives the nucleus a sharp contour and differentiates it clearly from the surrounding cytoplasm. This wall sometimes stains but very slightly, and can scarcely be differentiated from the outlying cytoplasm. In other and perhaps more frequent cases, it approaches in staining capacity the chromatin.

b. The *nuclear reticulum*. This, the most essential part of the nucleus, forms an irregular branching network or *reticulum* which consists of two very different constituents. The first of these, forming the general protoplasmic basis of the nucleus, is a substance known as *linin*

---

[1] Calkins, '98, I.

(Schwarz), invisible until after treatment by reagents, which in sections shows a finely granular structure and stains like the cytoplasmic substance, to which it is nearly related chemically (Figs. 7, 49). The second constituent, a deeply staining substance known as *chromatin* (Flemming), is the nuclear substance *par excellence*, for in many cases it appears to be the only element of the nucleus that is directly handed on by division from cell to cell, and it seems to have the power to produce all the other elements. The chromatin often appears in the form of scattered granules and masses of differing size and form, which are embedded in and supported by the linin-substance (Figs. 7, 19). In some cases the entire chromatin-content of the nucleus appears to be condensed into a single mass which simulates a nucleolus; for example, in *Spirogyra* and in various flagellates and rhizopods (e.g. *Actinosphærium*, *Arcella*); or there may be several such chromatin-masses, as in some of the Foraminifera and in *Noctiluca*. More commonly the chromatin forms a more or less regular network intermingled with and more or less embedded in the linin, from which it is often hardly distinguishable until the approach of mitosis, when a condensation of the chromatin-substance occurs.

In contradistinction to the other nuclear elements, chromatin is not acted upon, or is but slowly affected, by peptic digestion. It may thus be easily isolated for chemical analysis, which shows it to consist mainly of *nuclein*, *i.e.* a compound in varying proportions of a complex phosphorus-containing acid known as *nucleinic acid*, with albuminous bodies such as histon, protamin, or in some cases albumin itself.[1] Upon this, as will be shown in Chapter VI., probably depends the pronounced staining capacity when treated with the so-called "nuclear stains" (*e.g.* hæmatoxylin, methyl-green, and the basic tar-colours generally) from which chromatin takes its name. This capacity always increases as the nucleus prepares for division, reaching a climax in the spireme- and chromosome-stages, and it is also very marked in condensed nuclei such as those of spermatozoa. These variations are almost certainly due to varying proportions in the constituents of the nuclein, the staining capacity standing in direct ratio to the amount of nucleinic acid.

c. The *nucleoli*, one or more larger rounded or irregular bodies, suspended in the network, and staining intensely with many dyes. In some nuclei they are entirely absent. When present the nucleoli vary in number from one to five or more; and the number is often inconstant in the same species of cell, and even varies in the same cell with varying physiological conditions. In the eggs of some animals, at certain periods of growth (*e.g.* lower vertebrates), the nucleus may contain hundreds of nucleoli. An interesting case is that of the subcutaneous gland-cells of *Pisciola*, the nuclei of which contain in early phases of secretion but a single nucleolus. During growth of the cell the nucleolus fragments, finally giving rise to several hundred nucleoli which then appear to migrate out into the cytoplasm, leaving but a single nucleolus to repeat the cycle.[1]

---

[1] See p. 334.

The bodies known as nucleoli are of at least two different kinds. The first of these, the so-called true nucleoli or *plasmosomes* (Figs. 6, 8, *B*, 13), are of spherical form, and are shown by the staining reactions to differ widely from chromatin, being in general sharply stained by dyes which, like eosin, orange or acid fuchsin, stain the linin and the general cytoplasm. The plasmosomes sometimes seem to have no envelope, but in many cases (*e.g.* in leucocytes) are surrounded by a thin layer that stains like chromatin. Nucleoli of a quite different type are the "net-knots" (Netzknoten), chromatin-nucleoli, or *karyosomes*, which agree in staining reaction with chromatin and are doubtless to be regarded as merely a portion of the chromatin-network (Figs. 8, 49). These are sometimes spherical, more often irregular (Fig. 8), and often are hardly to be distinguished, except in size, from nodes of the chromatin-reticulum.[2] The relations between these two forms of nucleoli are far from certain, and the variations in staining reaction shown by true nucleoli render it not improbable that intermediate forms exist which may represent an actual transition from one to the other.[3] In many of the Protozoa, as described beyond, the "nucleolus" is shown by its behaviour during mitosis to be comparable with an attraction-sphere or centrosome ("nucleolo-centrosome," Keuten); and even in higher forms there are some cells in which the centrosome is intranuclear (Fig. 148).

There is good reason to believe that the chromatin-nucleoli are merely more condensed portions of the chromatin-network, since during cell-division they have the same history as the remaining portion of the chromatin-substance.[4] The nature of the true nucleoli is still imperfectly known. By some observers, including Flemming, O. and R. Hertwig, and Carnoy, they have been regarded as storehouses of material (para-nuclein, plastin) which contributes to the formation of chromosomes during division, and hence may play an active *rôle* in the nuclear activity. Strasburger ('95) likewise believes them to contain a store of active material which, however, has no direct relation to the chromosomes but consists of "kinoplasm" (p. 322), from which arises the achromatic part of the division-figure (p. 82). On the other hand, Häcker ('95, '99) and other observers regard the nucleolar material as a passive by-product of the chromatin-activity destined to be absorbed by the active sub-

---

[1] Montgomery, '98, 2.

[2] Flemming first called attention to the chemical difference between the true nucleoli and the chromatic reticulum ('82, pp. 138, 163) in animal-cells, and Zacharias soon afterward studied more closely the difference of staining reaction in plant-cells, showing that the former are especially coloured by alkaline carmine solutions, the latter by acid solutions. Other studies by Carnoy, Zacharias, Ogata, Rosen, Schwarz, Heidenhain, and many others show that the medullary substance (pyrenin) of true nuclei is coloured by acid tar-colours and other plasma stains, while the chromatin has a special affinity for basic dyes. *Cf.* p. 337.

[3] For very full review of the literature of the nucleoli see Montgomery ('98, 2).

[4] *Cf.* p. 67.

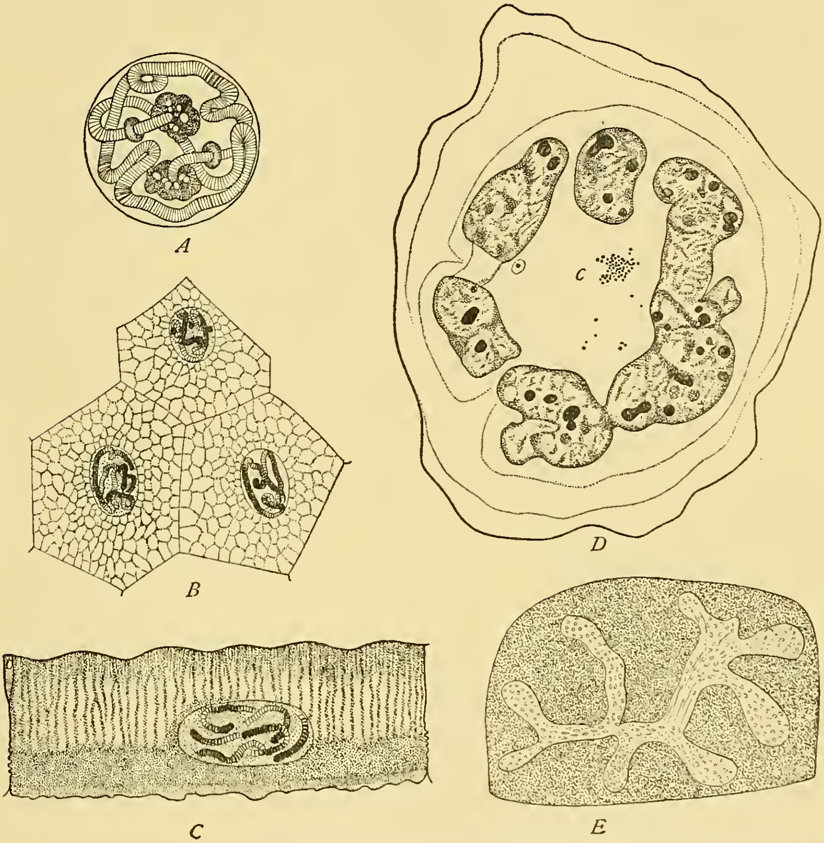

Fig. 14. — Special forms of nuclei.

A. Permanent spireme-nucleus, salivary gland of *Chironomus* larva. Chromatin in a single thread, composed of chromatin-discs (chromomeres), terminating at each end in a true nucleolus or plasmosome. [BALBIANI.]

B. Permanent spireme-nuclei, intestinal epithelium of dipterous larva *Ptychoptera.* [VAN GEHUCHTEN.] *C.* The same, side view.

D. Polymorphic ring-nucleus, giant-cell of bone-marrow of the rabbit; *c.* a group of centrosomes or centrioles. [HEIDENHAIN.]

E. Branching nucleus, spinning gland of butterfly-larva (*Pieris*). [KORSCHELT.]

stances. This is supported by the fact that in some forms of mitosis the nucleolus is at the time of division actually cast out of the nucleus into the cytoplasm, where it degenerates without further apparent function. This seems to constitute decisive evidence in support of Häcker's view as applied to certain cases; but without further evidence it must remain doubtful whether it applies to all.[1]

d. The *ground-substance*, *nuclear sap*, or *karyolymph*, a clear substance occupying the interspaces of the network and left unstained by most of the dyes that colour the chromatin, the linin, or the plasmosomes. By most observers the ground-substance is regarded as a liquid filling a more or less completely continuous space traversed by the nuclear network. By Bütschli, however, and some of his followers the nucleus is regarded as an alveolar structure, the walls of which represent the "network," while the ground-substance corresponds to the alveolar material. Nearly related with this is the view of Reinke ('94) that the ground-substance consists of large pale granules of "lanthanin" or "œdematin."

The configuration of the chromatic network varies greatly in different cases. It is sometimes of a very loose and open character, as in many epithelial cells (Fig. 1); sometimes extremely coarse and irregular, as in leucocytes (Fig. 49); sometimes so compact as to appear nearly or quite homogeneous, as in the nuclei of spermatozoa and in many Protozoa. In some cases the chromatin does not form a network, but appears in the form of a thread closely similar to the spireme-stage of dividing nuclei (*cf.* p. 65). The most striking case of this kind occurs in the salivary glands of dipterous larvæ (*Chironomus*), where, as described by Balbiani, the chromatin has the form of a single convoluted thread, composed of transverse discs and terminating at each end in a large nucleolus (Fig. 14, *A*). Somewhat similar nuclei (Fig. 14, *B*) occur in various epithelial cells of other insects (Van Gehuchten, Gilson), and also in the young ovarian eggs of certain animals (*cf.* p. 273). In certain gland-cells of the marine isopod *Anilocra* it is arranged in regular rosettes (Vom Rath). Rabl, followed by Van Gehuchten, Heidenhain, and others, has endeavoured to show that the nuclear network shows a distinct polarity, the nucleus having a "pole" toward which the principal chromatin-threads converge, and near which the centrosome lies.[2] In many nuclei, however, no trace of such polarity can be discerned.

The network may undergo great changes both in physical configuration and in staining capacity at different periods in the life of the same cell, and the actual amount of chromatin fluctuates, sometimes to an enormous extent. Embryonic cells are in general characterized by the large size of the nucleus; and Zacharias has shown in the case of plants that the nuclei of meristem and other embryonic tissues are not only relatively large, but contain a larger percentage of chromatin than in later stages. The relation of these changes to the physiological activity of the nucleus is still imperfectly understood.[1]

---

[1] *Cf.* pp. 126–130.

[2] *Cf.* the polarity of the cell, p. 55.

2. *Finer Structure of the Nucleus*

A considerable number of observers have raised the question whether the nuclear structures may not be regarded as aggregates of more elementary morphological bodies, though there is still no general agreement regarding their nature and relationships. The most definite evidence in this direction relates to the chromatic network. In the stages preparatory to division this network resolves itself into a definite number of rod-shaped bodies known as *chromosomes* (Fig. 21), which split lengthwise as the cell divides. These bodies arise as aggregations of minute rounded bodies or microsomes to which various names have been given (*chromomeres*, Fol; *ids*, Weismann). They are as a rule most clearly visible and most regularly arranged during cell-division, when the chromatin is arranged in a thread (*spireme*), or in separate *chromosomes* (Figs. 8, *D*, 53, *B*); but in many cases they are distinctly visible in the reticulum of the "resting" nucleus (Fig. 54). It is, however, an open question whether the chromatin-granules of the reticulum are individually identical with those forming the chromosomes or the spireme-thread. The larger masses of the reticu-

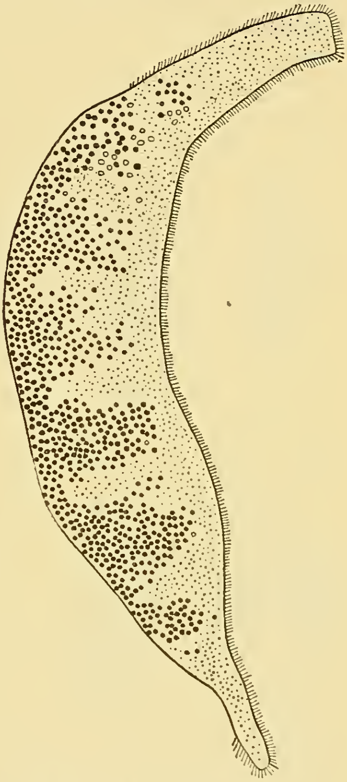

Fig. 15. — An infusorian, *Trachelocerca*, with diffused nucleus consisting of scattered chromatin-granules. [GRUBER.]

---

[1] Both chromatin-granules and nucleoli have been seen in a considerable number of living cells (Fig. 9). Favourable objects for this purpose are according to Korschelt ('96) the silk-glands of caterpillars, where the whole nucleus may be seen to be filled with fine granules ("microsomes"), among which are scattered many larger granules ("macrosomes"). The later studies of Meves ('97, 1) make it probable that the latter are true nucleoli and the former chromatin-granules. Korschelt, however, regards the "macrosomes" as composed of chromatin and the "microsomes" as representing the so-called "achromatic substance."

lum undoubtedly represent aggregations of such granules, but whether the latter completely fuse or remain always distinct is unknown. Even the chromosomes at certain stages appear perfectly homogeneous, and the same is sometimes true of the entire nucleus, as in the spermatozoön. It is nevertheless possible that the chromatin-granules have a persistent identity and are to be regarded as morphological units of which the chromatin is built up.[1]

Heidenhain ('93, '94), whose views have been accepted by Reinke, Waldeyer, and others, has shown that the "achromatic" nuclear network is likewise composed of granules, which he distinguishes as *lanthanin-* or *oxychromatin*-granules from the *basichromatin*-granules of the chromatic network. Like the latter, the oxychromatin-granules are suspended in a non-staining clear substance, for which he reserves the term *linin.* Both forms of granules occur in the chromatic network, while the achromatic network contains only oxychromatin. They are sharply differentiated by dyes, the basichromatin being coloured by the basic tar-colours (methyl-green, saffranin, etc.) and other true "nuclear stains"; while the oxychromatin-granules, like many cytoplasmic structures, and like the substance of true nucleoli (pyrenin), are coloured by acid tar-colours (rubin, eosin, etc.) and other "plasma stains." This distinction, as will appear in Chapter VII., is possibly one of great physiological significance.

Still other forms of granules have been distinguished in the nucleus by Reinke ('94) and Schloter ('94). Of these the most important are the "œdematin-granules," which according to the first of these authors form the principal mass of the ground-substance or "nuclear sap" of Hertwig and other authors. These granules are identified by both observers with the "cyanophilous granules," which Altmann regarded as the essential elements of the nucleus. It is at present impossible to give a consistent interpretation of the morphological value and physiological relations of these various forms of granules. The most that can be said is that the basichromatin-granules are probably normal structures; that they play a principal *rôle* in the life of the nucleus; that the oxychromatin-granules are nearly related to them; and that not improbably the one form may be transformed into the other in the manner suggested in Chapter VII.

The nuclear membrane is not yet thoroughly understood, and much discussion has been devoted to the question of its origin and structure. The most probable view is that long since advocated by Klein ('78) and Van Beneden ('83) that the membrane arises as a condensation of the general protoplasmic substance, and is part of the same structure as the linin-network and the cytoplasmic meshwork. Like these, it is in some cases "achromatic," but in other cases it shows the same staining reactions as chromatin, or may be double, consisting of an outer achromatic and an inner chromatic layer. According to Reinke, it consists of oxychromatin-granules like those of the linin-network.

---

[1] *Cf.* Chapter VI.

Interesting questions are raised by a comparison of these facts with the conditions observed in some of the lowest organisms, such as the flagellates and lower rhizopods among animals and the Cyanophyceæ and Bacteria among plants. In many of these forms (Fig. 16) no distinct nucleus can be demonstrated, the cell consisting of a mass of protoplasm in which are scattered numerous deeply staining granules. Many of these granules stain intensely with hæmatoxylin and other "nuclear" dyes; like chromatin, they resist the action of peptic digestion, and in at least one case (the bacterium-like *Achromatium*, according to Schewiakoff, '93) they have the power of division like the chromatin-granules of higher forms. For these

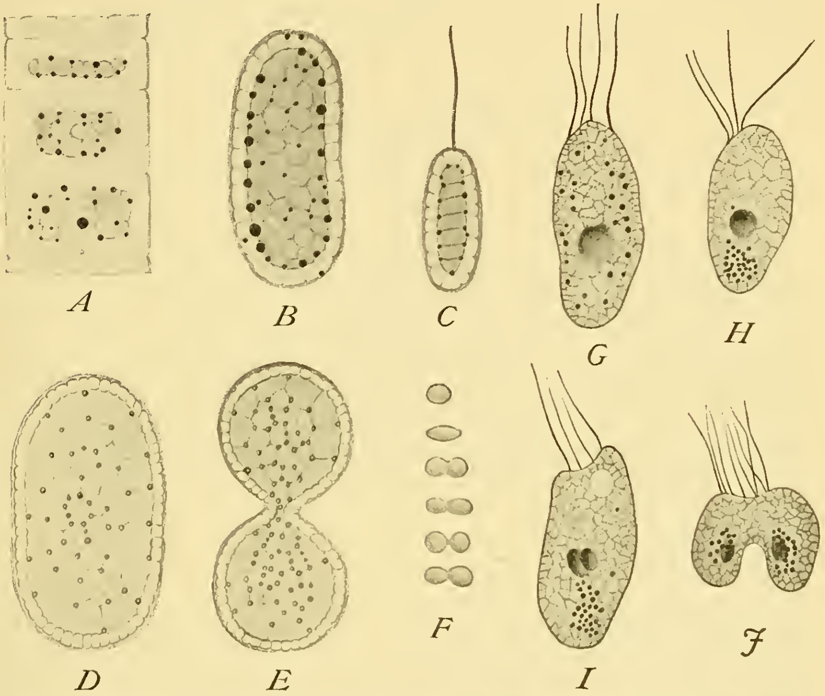

Fig. 16. — Forms of Cyanophyceæ, Bacteria, and Flagellates showing the so-called scattered or distributed nuclei. [*A–C.* BÜTSCHLI; *D–F.* SCHEWIAKOFF; *G–J.* CALKINS.]

A. Oscillaria. B. Chromatium. C. Bacterium lineola. D. Achromatium. E. The same in division. *F.* Fission of the granules. *G. Tetramitus,* with central sphere and scattered granules. *H.* Aggregation of the granules. *I.* Division of the sphere. *J.* Fission of the cell.

reasons most observers (Bütschli, Gruber, Schewiakoff, Nadson, etc.) regard them as true chromatin-granules which represent a scattered or distributed nucleus not differentiated as a definite morphological body. If this identification is correct, such forms probably give us the most primitive condition of the nuclear substance, which only in higher forms is collected into a distinct mass enclosed by a membrane; and the scattered granules are comparable to those forming the chromatin-reticulum and chromosomes in the higher types. The identification is, however, difficult, owing to the impossibility of actual chemical analysis; and Fischer ('97) has shown in the case of the Bacteria and Cyanophyceæ that we cannot safely trust either the staining reactions or the digestion test, since the former are variable, while the latter does not differentiate the granules from some other cytoplasmic constituents.[1] It is, however, certain that the staining power of chromatin in the higher forms varies with different conditions, and furthermore there is reason to believe that these granules may divide by fission. Besides these observations of Schewiakoff on *Achromatium* (see above), we have those of several authors on Infusoria, and more recently those of Calkins on flagellates, both pointing to the same conclusion. Balbiani, Gruber, Maupas, and others have described various Infusoria (*Urostyla, Trachelocerca, Holosticha, Uroleptus*), as well as some rhizopods (*Pelomyxa*), in which the body contains very numerous minute chromatin-granules of "nuclei" (Fig. 15), which Gruber ('87) showed to multiply by division. Balbiani ('61) long since showed that in *Urostyla* these bodies become concentrated toward the centre of the cell at the time of division, and Bergh ('89) demonstrated that they then fuse to form a macronucleus of the usual type, that elongates, assumes a fibrillar structure, and divides by fission. After division of the cell-body the macronucleus again fragments into minute scattered granules, which in this case certainly represent a distributed nucleus. In the flagellate *Tetramitus* Calkins ('98, 1) likewise finds numerous scattered chromatin-granules, which at the time of division become aggregated into a single dividing mass (p. 92); while in other forms the mass (nucleus) persists as such without (*Trachelomonas, Lagenella, Chilomonas*) or with (*Euglena, Synura*) a surrounding membrane.

Taken together, the foregoing facts, while certainly not conclusive, give good ground for the provisional acceptance of Bütschli's conception of the distributed nucleus, and indicate that nucleus and cytoplasm have arisen through the differentiation of a common protoplasmic mass. The nucleus, as Carnoy has well said,[2] is like a house built to contain the chromatic elements, and its achromatic elements (linin, etc.) were originally a part of the general cell-substance. Moreover, as Carnoy points out, the house periodically goes to pieces in the process of mitotic division, the chromatin afterward "building for itself a new dwelling."

---

[1] It should be remembered that we have no unerring "chromatin-stain." *Cf.* p. 335.

[2] '84, p. 251.

3. *Chemistry of the Nucleus*

The chemical nature of the various nuclear elements will be considered in Chapter VII., and a brief statement will here suffice. The following classification of the nuclear substances, proposed by Schwarz in 1887, has been widely accepted, though open to criticism on various grounds.

1. *Chromatin.* The chromatic substance (basichromatin) of the network and of those nucleoli known as net-knots or karyosomes.
2. *Linin.* The achromatic network and the spindle-fibres arising from it.
3. *Paralinin.* The ground-substance.
4. *Pyrenin* or *Parachromatin.* The inner mass of true nucleoli.
5. *Amphipyrenin.* The substance of the nuclear membrane.

Chromatin is probably identical with *nuclein* (p. 332), which is a compound of *nucleinic acid* (a complex organic acid, rich in phosphorus) and albuminous substances. In certain cases (nuclei of spermatozoa, and probably also the chromosomes at the time of mitosis) the percentage of nucleinic acid is very large (p. 333). The *linin* is supposed to be composed of "plastin"—a substance identified by Reinke and Rodewald ('81) and probably a nucleo-albumin or a related substance. "Pyrenin" is related to plastin; and Carnoy and Zacharias apply the latter word to the nucleolar substance, while O. Hertwig calls it paranuclein. "Amphipyrenin" has no very definite meaning; for the nuclear membrane sometimes appears to be of the same nature as the linin, while in other cases it stains like chromatin. For critique of the staining reactions see page 334.

D. THE CYTOPLASM

It has long been recognized that in the unicellular forms the cytoplasmic substance is often differentiated into two well-marked zones: viz. an inner medullary substance or *endoplasm* in which the nucleus lies, and an outer cortical substance or *exoplasm* (ectoplasm) from which the more differentiated products of the cytoplasm, such as cilia, trichocysts, and membrane, take their origin. Indications of a similar differentiation are often shown in the tissue-cells of higher plants and animals,[1] though it may take the form of a polar differentiation of the cell-substance, or may be wholly wanting. Whether the distinction is of fundamental importance remains to be seen; but it appears to be a general rule that the nucleus is surrounded by protoplasm of relatively slight differentiation, while the more highly differentiated products of cell-activity are laid down in the more peripheral region of the cell, either in the cortical zone or at one end of the cell.[1] This fact is full of meaning, not only because it is an expression of the adaptation of the cell to its external environment, but also because of its bearing on the problems of nutrition.[2] For if, as we shall see reason to conclude in Chapter VII., the nucleus be immediately concerned with synthetic metabolism, we should expect to find the immediate and less differentiated products of its action in its neighbourhood, and on the whole the facts bear out this view.

---

[1] This fact was first pointed out in the tissue-cells of animals by Kupffer ('75), and its importance has since been urged by Waldeyer, Reinke, and others. The cortical layer is by Kupffer termed *paraplasm*, by Pfeffer *hyaloplasm*, by Pringsheim the *Hautschicht*. The medullary zone is termed by Kupffer *protoplasm, sensu strictu;* by Strasburger, *Körnerplasma;* by Nägeli, *polioplasm*.

The most pressing of all questions regarding the cytoplasmic structure is whether the sponge-like, fibrillar, or alveolar appearance is a normal condition existing during life. There are many cases, especially among plant-cells, in which the most careful examination has thus far failed to reveal the presence of a reticulum, the cytoplasm appearing, even under the highest powers and after the most careful treatment, merely as a finely granular substance. This and the additional fact that the cytoplasm may show active streaming and flowing movements, has led some authors, especially among botanists, to regard the reticulum as non-essential and as being, when present, either a secondary differentiation of the cytoplasmic substance specially developed for the performance of particular functions or a mere coagulation-product due to the action of fixatives. It has been shown that structureless proteids, such as egg-albumin and other substances, when coagulated by various reagents, often show a structure closely similar to that of protoplasm as observed in microscopical sections. Flemming ('82) long since called attention to the danger of mistaking such coagulation-products for normal structures as seen in fixed and stained material, and his warning has been emphasized by the later experiments of Berthold ('86), Schwarz ('87), and especially of Bütschli ('92, '98), Fischer ('94, '95, '99), and Hardy ('99). Bütschli's extensive studies of such coagulation-phenomena show that coagulated or dried albumin, starch-solutions, gelatin, gum arabic, and other substances show a fine alveolar structure scarcely to be distinguished from that which he believes to be the normal and typical structure of protoplasm. Fischer and Hardy have likewise made extensive tests of solutions of albumin, peptone, and related substances, in various degrees of concentration, fixed and stained by a great variety of the reagents ordinarily used for the demonstration of cell-structures. The result was to produce a marvellously close *simulacrum* of the appearances observed in the cell, alveolar, reticulated, and fibrillar structures being produced that often contain granules closely similar in every respect to those described as

---

[1] *Cf.* p. 55.

[2] See Kupffer ('90), pp. 473–476.

"microsomes" in sections of actual protoplasm. After impregnating pith with peptone-solution and then hardening, sectioning, and staining, the cells may even contain a central nucleus-like mass suspended in a network of anastomosing threads that extend in every direction outward to the walls, and give a remarkable likeness of a normal cell.

These facts show how cautious we must be in judging the appearances seen in preserved cells, and justify in some measure the hesitation with which many existing accounts of cell-structure are received. The evidence is nevertheless overwhelmingly strong, as I believe, that not only the fibrillar and alveolar formations, but also the microsomes observed in cell-structures, are in part normal structures. This evidence is derived partly from a study of the living cell, partly from the regular and characteristic arrangement of the thread-work and

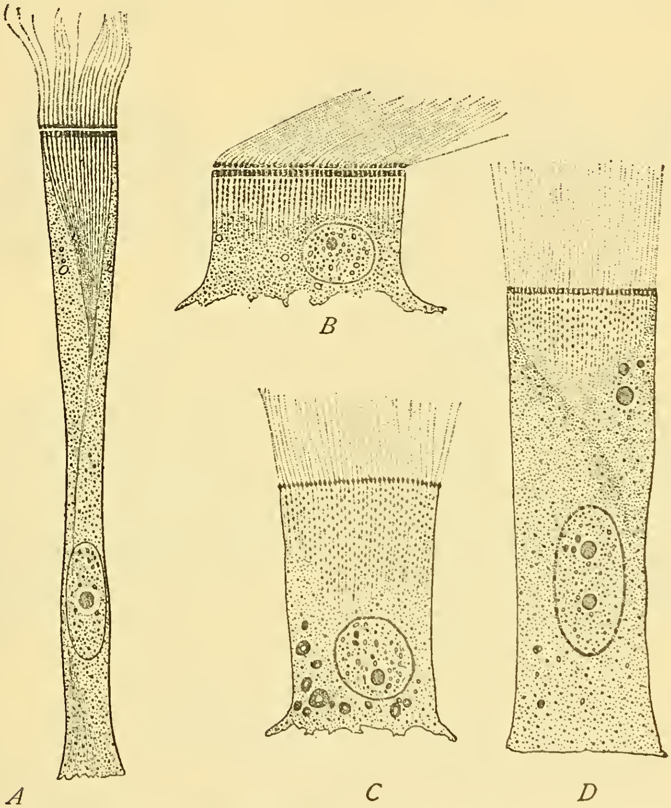

Fig. 17. — Ciliated cells, showing cytoplasmic fibrillæ terminating in a zone of peripheral microsomes to which the cilia are attached. [ENGELMANN.]

A. From intestinal epithelium of *Anodonta*. *B*. From gill of *Anodonta*. *C.D.* Intestinal epithelium of *Cyclas*.

microsomes in certain cases. In many Protozoa, for example, a fine alveolar structure may be seen in the living protoplasm; and Flemming as well as many later observers has clearly seen fibrillar structures in the living cells of cartilage, epithelium connective-tissue, and some other animal cells (Fig. 9). Mikosch, also, has recently described *granular* threads in living plant-cells.

Almost equally conclusive is the beautifully regular arrangement of the fibrillæ in ciliated cells (Fig. 17, Engelmann), in muscle-fibres and nerve-fibres, and especially in the mitotic figure of dividing cells (Figs. 21, 31), where they are likewise more or less clearly visible in life. A very convincing case is afforded by the pancreas-cells of *Necturus*, which Mathews has carefully studied in my laboratory. Here the thread-work consists of long, conspicuous, definite fibrillæ, some of which may under certain conditions be wound up more or less closely in a spiral mass to form the so-called *Nebenkern*. In all these cases it is impossible to regard the thread-work as an accidental coagulation-product. In the case of echinoderm eggs, I have made ('99) a critical comparison of the living structure, as seen under powers

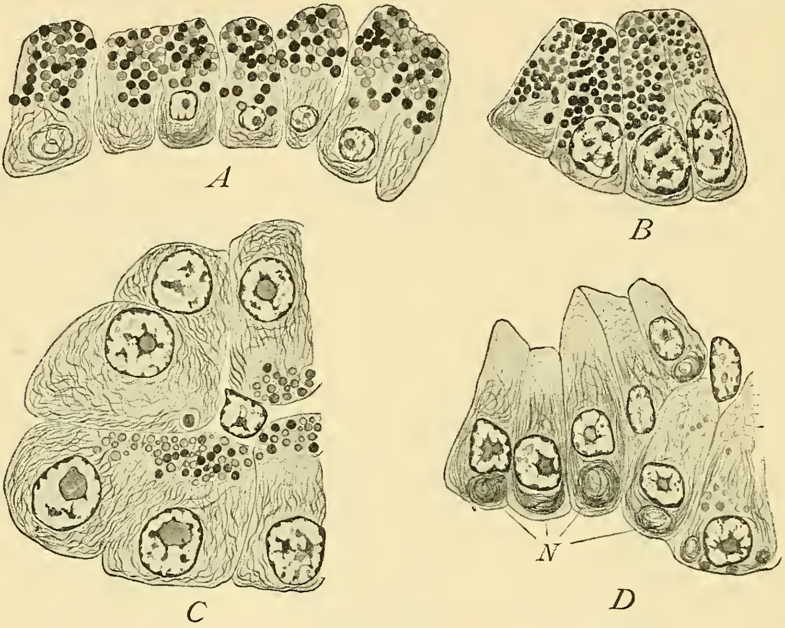

Fig. 18. — Cells of the pancreas in Amphibia. [MATHEWS.]

A–C. *Necturus;* D. *Rana.* A and B represent two stages of the "loaded" cell, showing zymogen-granules in the peripheral and fibrillar structures in the basal part of the cell. C shows cells after discharge of the granule-material and invasion of the entire cell by fibrillæ. In D portions of the fibrillar material are coiled to form the mitosome ("paranucleus" or "Nebenkern").

of a thousand diameters and upwards, with the same object stained in thin sections after fixation by picro-acetic, sublimate-acetic, and

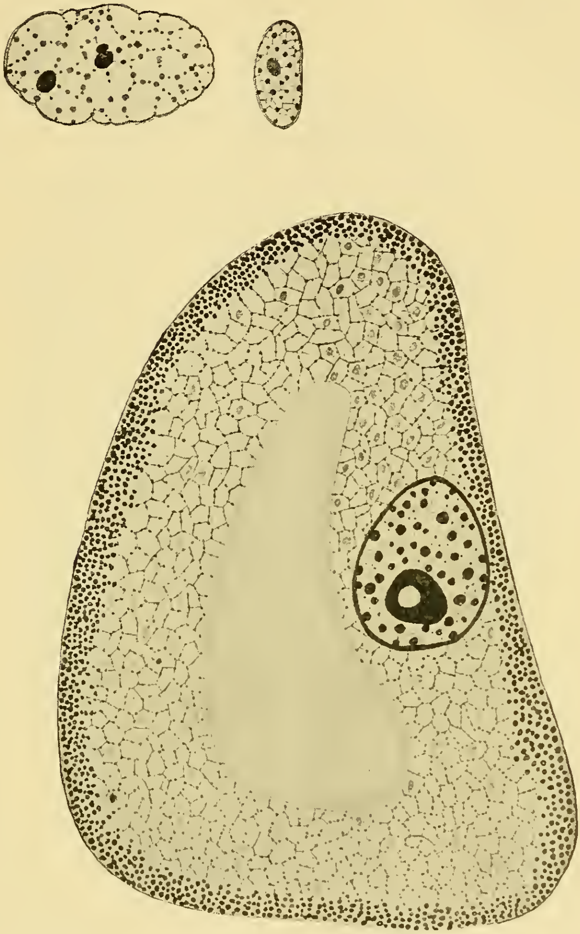

Fig. 19. — Section through a nephridial cell of the leech, *Clepsine* (drawn by Arnold Graf from one of his own preparations).

The centre of the cell is occupied by a large vacuole, filled with a watery liquid. The cytoplasm forms a very regular and distinct reticulum with scattered microsomes which become very large in the peripheral zone. The larger pale bodies, lying in the ground-substance, are excretory granules (*i.e.* metaplasm). The nucleus, at the right, is surrounded by a thick chromatic membrane, is traversed by a very distinct linin-network, contains numerous scattered chromatin-granules, and a single large nucleolus within which is a vacuole. Above are two isolated nuclei showing nucleoli and chromatin-granules suspended in the linin-threads.

other reagents. The comparison leaves no doubt that the normal structures are in this case very perfectly preserved, though the sections give at first sight an appearance somewhat different from that of the living object, owing to differences of staining capacity. In these eggs the microsomes, thickly scattered through the alveolar walls, stain deeply (Figs. 11, 12), while the alveolar spheres hardly stain at all. When, therefore, the stained sections are cleared in balsam, the contours of the alveolar spheres almost disappear, and the eye is caught by the walls, which give at first sight quite the appearance of a granular reticulum, as it has been in fact described by many observers. Careful study of the sections shows, however, that *the form and arrangement of all the elements is almost identically the same as in life.*

This result shows that careful treatment by reagents in some cases at least gives a very faithful picture of the normal structure; and while it should never be forgotten that in sections we are viewing coagulated material, much of which is liquid or semi-liquid in life, we should not adopt too pessimistic a view of the results based on fixed material, as I think some of the experimenters referred to above have done. Wherever possible, the structures observed in sections should be compared with those in the living material. When this is impracticable we must rely on indirect evidence; but this is in many cases hardly less convincing than the direct.

It is a very interesting and important question whether living protoplasm that appears to the eye to be homogeneous does not really possess a structure that is invisible, owing to the extreme tenuity of the fibrillæ or alveolar walls (as was long since suggested by Heitzmann and Bütschli),[1] or to uniformity of refractive index in the structural elements. It is highly probable that such is often the case; indeed, Bütschli has shown that such "homogeneous" protoplasm in Protozoa may show a typical alveolar structure after fixation and staining. This explanation will not, however, apply to the young echinoderm eggs (already referred to at p. 28), where the genesis of the alveolar structure may be followed step by step in the living cell. The protoplasm here appears at first almost like glass, showing at most a sparse and fine granulation; but after fixing and staining it appears as a mass of fine, closely crowded granules. This may indicate the existence of an extremely fine alveolar structure in life; but on the whole I believe that these granules are for the most part coagulation-products, since they cannot be demonstrated by staining *intra vitam*, and they very closely resemble the coagulation-granules found in structureless proteids like egg-albumin after treatment by the same reagents. In common with many other investigators, therefore, I believe that protoplasm may in fact be homogeneous *down to the present limits of microscopical vision.*

One of the must beautiful forms of cyto-reticulum with which I am acquainted has been described by Bolsius and Graf in the nephridial cells of leeches as shown in Fig. 19 (from a preparation by Dr. Arnold Graf). The meshwork is here of great distinctness and regularity, and scattered microsomes are found along its threads. It appears with equal clearness, though in a somewhat different form, in many eggs, where the meshes are rounded and often contain food-matters or deutoplasm in the inter-spaces (Figs. 59, 60). In cartilage-cells and connective tissue-cells, where the threads can be plainly seen

---

[1] *Cf.* Bütschli, '92, 2, p. 169.

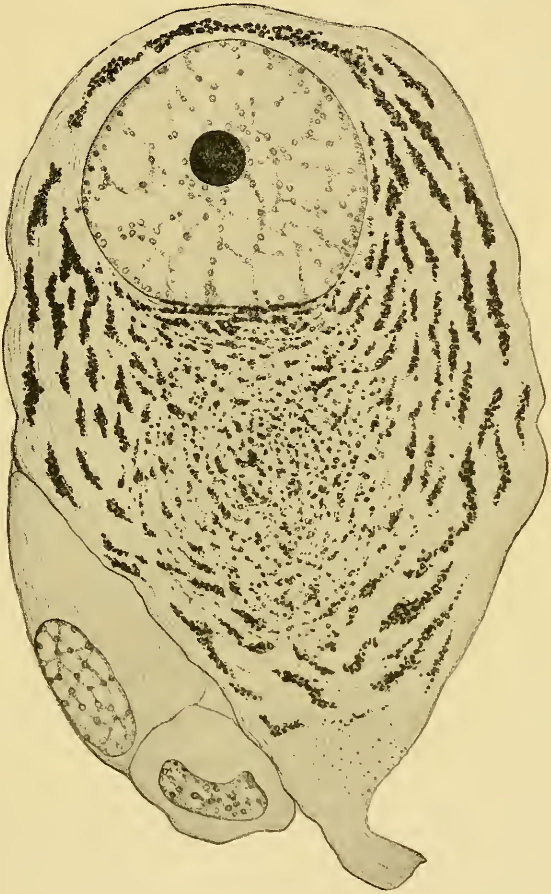

Fig. 20. — Spinal ganglion-cell of the frog. [Lenhossék.]

The nucleus contains a single intensely chromatic nucleolus, and a paler linin-network with rounded chromatin-granules. The cytoplasmic fibrillæ are faintly shown passing out into the nerve-process below. (They are figured as far more distinct by Flemming.) The dark cytoplasmic masses are the deeply staining "chromophilic granules" (Nissl) of unknown function. (The centrosome, which lies near the centre of the cell, is shown in Fig. 8, *C*.) At the left, two connective tissue-cells.

in life, the network is loose and open, and appears to consist of more or less completely separate threads (Fig. 9). In the cells of columnar epithelium, the threads in the peripheral part of the cell often assume a more or less parallel course, passing outwards from the central region, and giving the outer zone of the cell a striated appearance. This is very conspicuously shown in ciliated epithelium, the fibrillæ corresponding in number with the cilia as if continuous with their bases (Fig. 17).[1] In nerve-fibres the threads form closely set parallel fibrillæ which may be traced into the body of the nerve-cell; here, according to most authors, they break up into a network in which are suspended numerous deeply staining masses, the "chromophilic granules" of Nissl (Fig. 20).[2] In the contractile tissues the threads are in most cases very conspicuous and have a parallel course. This is clearly shown in smooth muscle-fibres and also, as Ballowitz has shown, in the tails of spermatozoa. This arrangement is most striking in striped muscle-fibres where the fibrillæ are extremely well marked. According to Retzius, Carnoy, Van Gehuchten, and others, the meshes have here a rectangular form, the principal fibrillæ having a longitudinal course and being connected at regular intervals by transverse threads; but the structure of the muscle-fibre is probably far more complicated than this account would lead one to suppose, and opinion is still divided as to whether the contractile substance is represented by the reticulum proper or by the ground-substance.

Nowhere, perhaps, is a fibrillar structure shown with such beauty as in dividing cells, where (Figs. 21, 31) the fibrillæ group themselves in two radiating systems or *asters*, which are in some manner the immediate agents of cell-division. Similar radiating systems of fibres occur in amœboid cells, such as leucocytes (Fig. 49) and pigment-cells (Fig. 50), where they probably form a contractile system by means of which the movements of the cell are performed.

The views of Bütschli and his followers, which have been touched on at p. 25, differ considerably from the foregoing, the fibrillæ being regarded as the optical sections of thin plates or lamellæ which form the walls of closed chambers filled by a more liquid substance. Bütschli, followed by Reinke, Eismond, Erlanger, and others, interprets in the same sense the astral systems of dividing cells which are regarded as a radial configuration of the lamellæ about a central point (Fig. 10, *B*). Strong evidence against this view is, I believe, afforded by the appearance of the spindle and asters in cross-section. In the early stages of the egg of *Nereis*, for example, the astral rays are coarse anastomosing fibres that stain intensely and are therefore very favourable for observation (Fig. 60). That they are actual fibres is, I think, proved by sagittal sections of the asters in which the rays are cut at various angles. The cut ends of the branching rays appear in the clearest manner, not as plates but as distinct dots, from which in oblique sections the ray may be traced inwards toward the centrosphere. Drüner, too, figures the spindle in cross-section as consisting of rounded dots, like the end of a bundle of wires, though these are connected by cross-branches (Fig. 28, *F*). Again, the crossing of the rays proceeding from the asters (Fig. 128), and their behaviour in certain phases of cell-division, is difficult to explain under any other than the fibrillar theory.

---

[1] The structure of the ciliated cell, as described by Engelmann, may be beautifully demonstrated in the funnel-cells of the nephridia and sperm-ducts of the earthworm.

[2] The remarkable researches of Apathy ('97) on the nerve-cells of leeches have revealed the existence within the nerve-cell of networks far more complex and definite than was formerly supposed, and showing definite relations to incoming and outgoing fibrillæ within the substance of the nerve-fibres.

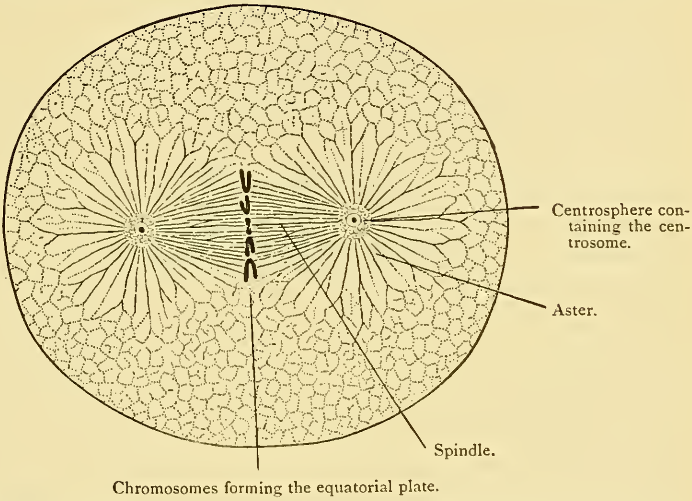
Centrosphere containing the centrosome.
Aster.
Spindle.
Chromosomes forming the equatorial plate.

Fig. 21. — Diagram of the dividing cell, showing the mitotic figure and its relation to the cytoplasmic meshwork.

We must admit, however, that the meshwork varies greatly in different cells and even in different physiological phases of the same cell; and that it is impossible at present to bring it under any rule of universal application. It is possible, nay probable, that in one and the same cell a portion of the meshwork may form a true alveolar structure such as is described by Bütschli, while other portions may, at the same time, be differentiated into actual fibres. If this be true the fibrillar or alveolar structure is a matter of secondary moment, and the essential features of protoplasmic organization must be sought in a more subtle underlying structure.[1]

---

[1] See Chapter VI.

Space would not suffice for a comparative account of the endless modifications shown by the cytoplasmic substance in different forms of cells. Many of these arise through special differentiations of the active substance, the character of the structure thus being sometimes so highly modified, as in the striated muscle-fibre, that it is difficult to trace its exact relation to the more usual forms. More commonly the cytoplasm is modified through the formation of passive or metaplasmic substances which often completely transform the original appearance of the cell. The most frequent of such modifications arise through the deposit of liquid drops and "granules" (many of the latter, however, being no doubt liquid in life). When the liquid drops are of watery nature the cavities in which they lie are known as *vacuoles*, which are especially characteristic of the protoplasm of plant-cells and of Protozoa. These may enlarge or run together to form extensive cavities in the cell, the protoplasm becoming reduced to a peripheral layer, or to strands and networks traversing the spaces; while in some forms of unicellular glands the spaces may form branching canals traversing the protoplasm.

BOSTON MEDICAL LIBRARY
FEB 26 1910

The vacuolization or meshlike appearance arising through the formation of larger vacuoles or the deposit of other metaplasmic material is not to be confounded with the primary protoplasmic structure. When, however, smaller vacuoles or metaplasmic granules are evenly distributed through the protoplasm, a "pseudo-alveolar" structure (Reinke) arises that can often hardly be distinguished from the "true" alveolar structure of Bütschli.[1] Comparative study shows that all gradations exist between the "false" and the "true" alveolar structures and that no logical ground of distinction between the two exists.[2] We thus reach ground for the conclusion that the coarser secondary alveolar or reticular formations are to be regarded as only an exaggeration of the primary structure, and that the alveolar material of Bütschli's structure belongs in the same general category with the passive or metaplasmic substance.[3]

E. The Centrosome

The centrosome[4] is usually an extremely minute body, or more commonly a pair of bodies, staining intensely with hæmatoxylin and some other reagents, and surrounded by a cytoplasmic radiating aster or by a rounded mass known as the *attraction-sphere* (Figs. 8, 49, etc.). As a rule it lies in the cytoplasm, not far from the nucleus, and usually opposite an indentation or bay in the latter; but in a few cases it lies inside the nucleus (Fig. 148). In epithelia the centrosomes (usually double) lie as a rule near the free end of the cell (Fig. 23).[1]

---

[1] In the latter the alveolar spheres are, according to Bütschli, not more than one or two microns in diameter.

[2] This has been demonstrated in the cells of plants by *Crato* ('96), and more recently by the writer ('99), in the case of echinoderm and other eggs.

[3] *Cf.* p. 29.

[4] The centrosome was apparently first seen and described by Flemming in 1875, in the egg of the fresh-water mussel *Anodonta*, and independently discovered by Van Beneden, in

There is still much confusion regarding the relation of the centrosome to the surrounding structures, and this has involved a corresponding ambiguity in the terminology. We will therefore only consider it briefly at this point, deferring a more critical account to Chapter VI. In its simplest form it is a single minute granule, which may, however, become double or triple (leucocytes, connective tissue-cells, some epithelial cells) or even multiple, as in certain giant-cells (Fig. 14, *D*), and as also occurs in some forms of cell-division (Fig. 52). In some cases (Figs. 8, *C*, 120, 148) the "centrosome" is a larger body containing one or more central granules or "centrioles" (Boveri); but it is probable that in some of these cases the central granule is itself the true centrosome, and the surrounding body is part of the attraction-sphere. During the formation of the spermatozoön the centrosome undergoes some remarkable morphological changes (p. 171), and is closely involved in the formation of the contractile structures of the tail.

The nature and functions of the centrosome have formed the subject of some of the most persistent and searching investigations of recent cytology. Van Beneden, followed by Boveri and many later workers, regarded the centrosome as a distinct and persistent cell-organ, which like the nucleus was handed on by division from one cell-generation to another. Physiologically it was regarded as being the especial organ of cell-division, and in this sense as the "dynamic centre" of the cell. In Boveri's beautiful development of this

---

the following year, in dycyemids. The name is due to Boveri ('88, 2, p. 68). Van Beneden's and Boveri's independent identification of centrosome in *Ascaris* as a permanent cell-organ ('87) was quickly supported by numerous observations on other animals and on plants. In rapid succession the centrosome and attraction-sphere were found to be present in pigment-cells of fishes (Solger, '89, '90), in the spermatocytes of Amphibia (Hermann, '90), in the leucocytes, endothelial cells, connective tissue-cells, and lung-epithelium of salamanders (Flemming, '91), in various plant-cells (Guignard, '91), in the one-celled diatoms (Bütschli, '91), in the giant-cells and other cells of bone-marrow (Heidenhain, Van Bambeke, Van der Stricht, '91), in the flagellate *Noctiluca* (Ishikawa, '91), in the cells of marine algæ (Strasburger, '92), in cartilage-cells (Van der Stricht, '92), in cells of cancerous growths (epithelioma, Lustig and Galeotti, '92), in the young germ-cells as already described, in gland-cells (Vom Rath, '95), in nerve-cells (Lenhossék, '95), in smooth muscle-fibres (Lenhossék, '99), and in embryonic cells of many kinds (Heidenhain, '97). Many others have confirmed and extended this list. Guignard's identification of the centrosomes in higher plants is open to grave doubt (*cf.* p. 82).

[1] *Cf.* p. 57.

view it was regarded further as the especial fertilizing element in the spermatozoön, which, when introduced into the egg, endowed the latter with the power of division and development. Van Beneden's and Boveri's hypothesis, highly attractive on account of its simplicity and lucidity, is supported by many facts, and undoubtedly contains an element of truth; yet recent researches have cast grave doubt upon its generality, and necessitate a suspension of judgment upon the entire matter. Many of the most competent recent workers on the cytology of higher plants have been unable to find centrosomes, whether in the resting-cells, in the apparatus of cell-division, or during the process of fertilization, notwithstanding the fact that undoubted centrosomes occur in some of the lower plants. Among zoölogists, too, an increasing number of recent investigators, armed with the best technique, have maintained the total disappearance of the centrosome at the close of cell-division or during the process of fertilization, agreeing that in such cases the centrosome is subsequently formed *de novo*. Experimental researches, also, have given strong ground for the conclusion that cells placed under abnormal chemical conditions may form new centrosomes (p. 306). If these strongly supported results be well founded, Van Beneden's hypothesis must be abandoned in favour of the view that the centrosome is but a subordinate part of the general apparatus of mitosis, and one which may be entirely dispensed with. Thus regarded, the centrosome would lose somewhat of the significance first attributed to it, though still remaining a highly interesting object for further research.[1]

F. Other Organs

The cell-substance is often differentiated into other more or less definite structures, sometimes of a transitory character, sometimes showing a constancy and morphological persistency comparable with that of the nucleus and centrosome. From a general point of view the most interesting of these are the bodies known as *plastids* or *protoplasts* (Fig. 6), which, like the nucleus and centrosome, are capable of growth and division, and may thus be handed on from cell to cell. The most important of these are the *chromatophores* or *chromoplastids*, which are especially characteristic of plants, though they occur in some animals as well. These are definite bodies, varying greatly in form and size, which possess the power of growth and division, and have in some cases been traced back to minute colourless plastids or leucoplastids in the embryonic cells. By enlargement and differentiation these give rise to the starch-builders (amyloplastids), to the chlorophyll-bodies (chloroplastids), and to other pigment-bodies (chromoplastids), all of which may retain the power of division. The embryonic leucoplastids are also believed to multiply by division and to arise by the division of plastids in the parental organism; but it remains an open question whether this is their only mode of origin, and the same is true of the more highly differentiated forms of plastids to which they may give rise.

---

[1] *Cf.* pp. 111, 304. Eisen ('97) asserts that in the blood of a salamander, *Batrachoseps*, the attraction-sphere ("archosome") containing the centrosomes may separate from the remainder of the cell (nucleated red corpuscles) to form an independent form of blood-corpuscle or "plasmocyte," which leads an active life in the blood.

The contractile or pulsating vacuoles that occur in most Protozoa and in the swarm-spores of many Algæ are also known in some cases to multiply by division; and the same is true, according to the researches of De Vries, Went, and others, of the non-pulsating vacuoles of plant-cells. These vacuoles have been shown to have, in many cases, distinct walls, and they are regarded by De Vries as a special form of plastid ("tonoplasts") analogous to the chromatophores and other plastids. It is, however, probable that this view is only applicable to certain forms of vacuoles.

The plastids possess in some cases a high degree of morphological independence, and may even live for a time after removal from the remaining cell-substance, as in the case of the "yellow cells" of Radiolaria. This has led to the view, advocated by Brandt and others, that the chlorophyll-bodies found in the cells of many Protozoa and a few Metazoa (*Hydra*, *Spongilla*, some planarians) are in reality distinct Algæ living symbiotically in the cell. This view is probably correct in some cases, *e.g.* in the Radiolaria; but it may be doubted whether it is of general application. In the plants the plastids are almost certainly to be regarded as differentiations of the protoplasmic substance.

The existence of cell-organs which have the power of independent assimilation, growth, and division is a fact of great theoretical interest in its bearing on the general problem of cell-organization; for it is one of the main reasons that have led De Vries, Wiesner, and many others to regard the entire cell as made up of elementary self-propagating units.

G. THE CELL-MEMBRANE

The structure and origin of the cell-wall or membrane form a subject somewhat apart from our general purpose, since the wall belongs to the passive or metaplasmic products of protoplasm rather than to the living cell itself. We shall therefore treat it very briefly. Broadly speaking, animal cells are in general characterized by the slight development and relative unimportance of the cell-walls, while the reverse is the case in plants, where the cell-walls play a very important *rôle*. In the latter the wall sometimes attains a great thickness, usually displays a distinct stratification, and often has a complex sculpture. Such massive walls very rarely occur in the case of animal tissues, though the intercellular matrix of cartilage and bone is to a certain extent analogous to them, and the thick and often highly sculptured envelopes of some kinds of eggs and of various Protozoa may be placed in the same category.

It is open to question whether any cells are entirely devoid of an enclosing envelope; for even in such "naked" cells as leucocytes, rhizopods, or membraneless eggs, the boundary of the cell is usually formed by a more resistant layer of protoplasm or "pellicle" (Bütschli) which may be so marked as to simulate a true membrane, as is the case, for example, in the red blood-corpuscles (Ranvier, Waldeyer, etc.). Such pellicles probably differ from true membranes only in degree; but it is still an open question both in animals and in plants, how far true membranes arise by direct transformation of the peripheral protoplasmic layer (the "Hautschicht" of botanists), and how far as a secretion-product of the protoplasm. In the case of animal cells, Leydig long since proposed[1] to distinguish between "cuticular" membranes, formed as secretions and usually occurring only on the free surfaces (as in epithelia), from "true membranes" arising by direct transformation of the peripheral protoplasm. Later researches, including those of Leydig himself, have thrown so much doubt on this distinction that most later writers have used the term *cuticular* in a purely topographical sense to denote membranes formed only on one (the free) side of the cell,[2] leaving open the question of origin. The formation and growth of the cell-wall have been far more thoroughly studied in plants than in animals, yet even here opinion is still divided. Most recent researches tend to sustain the early view of Nägeli that the cell-wall is in general a secretion-product, though there are some cases in which a direct transformation of protoplasm into membrane-stuff seems to occur.[3] In the division of plant-cells the daughter-cells are in almost all cases cut apart by a cell-plate which arises in the protoplasm of the mother-cell as a transverse series of thickenings of the spindle-fibres in the equatorial region (Fig. 34). This fact, long regarded by Strasburger and others as a proof of the direct origin of the membrane from the protoplasmic substance, is shown by Strasburger's latest work ('98) to be open to a quite different interpretation, the actual wall being formed by a splitting of the cell-plate into two layers between which the wall appears as a secretion-product. Almost all observers further are agreed that the formation of new membranes on naked masses of protoplasm produced by plasmolysis are likewise secretion-products, and that the secondary thickening of plant-membranes is produced in the same way. These facts, together with the scanty available zoölogical data, indicate that the formation of membranes by secretion is the more usual and typical process.[1]

---

[1] *Cf.* '85, p. 12. [2] *Cf.* O. Hertwig, '93. [3] *Cf.* Strasburger, '98.

The chemical composition of the membrane or intercellular substance varies extremely. In plants the membrane consists of a basis of *cellulose*, a carbohydrate having the formula $C_6H_{10}O_5$; but this substance is very frequently impregnated with other substances, such as silica, lignin, and a great variety of others. In animals the intercellular substances show a still greater diversity. Many of them are nitrogenous bodies, such as keratin, chitin, elastin, gelatin, and the like; but inorganic deposits, such as silica and carbonate of lime, are common.

H. Polarity of the Cell

In a large number of cases the cell exhibits a definite polarity, its parts being symmetrically grouped with reference to an ideal *organic axis* passing from pole to pole. No definite criterion for the identification of the cell-axis has, however, yet been determined; for the general conception of cell-polarity has been developed in two different directions, one of which starts from purely morphological considerations, the other from physiological, and a parallelism between them has not thus far been fully made out.

On the one hand, Van Beneden ('83) conceived cell-polarity as a primary morphological attribute of the cell, the organic axis being identified as a line drawn through the centre of the nucleus and the centrosome (Fig. 22, *A*). With this view Rabl's theory ('85) of nuclear polarity harmonizes, for the chromosome-loops converge toward the centrosome, and the nuclear axis coincides with the cell-axis. Moreover, it identifies the polarity of the egg, which is so important a factor in development, with that of the tissue-cells; for the egg-centrosome almost invariably appears at or near one pole of the ovum.

Heidenhain ('94, '95) has recently developed this conception of polarity in a very elaborate manner, maintaining that all the structures of the cell have a definite relation to the primary axis, and that this relation is determined by conditions of tension in the astral rays focussed at the centrosome. On this basis he endeavours to explain the position and movements of the nucleus, the succession of division-planes, and many related phenomena.[1]

---

[1] Strasburger ('97, 3, '98) believes membrane-formation in general to be especially connected with the activity of the "kinoplasm," or filar plasm of which he considers the "Hautschicht," as well as the spindle-fibres, to be largely composed. In support of this may be mentioned, besides the mode of formation of the partition-walls in the division of plant-cells, Harper's ('97) very interesting observations on the formation of the ascospores in *Erysiphe* (Fig. 33), where the spore-membrane appears to arise directly from the astral rays.

Hatschek ('88) and Rabl ('89, '92), on the other hand, have advanced a quite different hypothesis based on physiological considerations. By "cell-polarity" these authors mean, not a predetermined morphological arrangement of parts in the cell, but a polar differentiation of the cell-substance arising secondarily through adaptation of the cell to its environment in the tissues, and having no necessary relation to the polarity of Van Beneden (Fig. 22, *B*, *C*). This is typically shown in epithelium, which, as Kölliker and Haeckel long since pointed out, is to be regarded, both ontogenetically and phylogenetically, as the most primitive form of tissue. The free and basal ends of the cells here differ widely in relation to the food-supply, and show a corresponding structural differentiation. In such cells the nucleus usually lies nearer the basal end, toward the source of food, while the differentiated products of cell-activity are formed either at the free end (cuticular structures, cilia, pigment, zymogen-granules), or at the basal end (muscle-fibres, nerve-fibres). In the non-epithelial tissues the polarity may be lost, though traces of it are often shown as a survival of the epithelial arrangement of the embryonic stages.

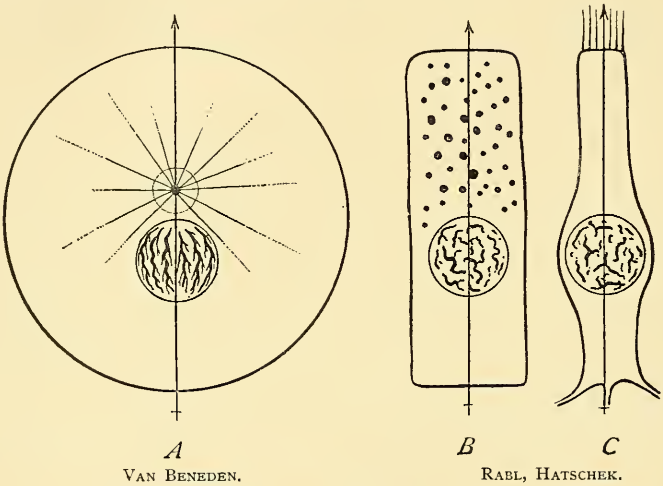

Fig. 22. — Diagrams of cell-polarity.

A. Morphological polarity of Van Beneden. Axis passing through nucleus and centrosome. Chromatin-threads converging toward the centrosome. *B.C.* Physiological polarity of Rabl and Hatschek, *B* in a gland-cell, *C* in a ciliated cell.

---

[1] *Cf.* p. 105.

But, although this conception of polarity has an entirely different point of departure from Van Beneden's, it leads, in some cases at least, to the same result; for the cell-axis, as thus determined, may coincide with the morphological axis as determined by the position of the centrosome. This is the case, for example, with both the spermatozoön and the ovum; for the morphological axis in both is also the physiological axis about which the cytoplasmic differentiations are grouped. Recent researches have further shown that the same is the case in many forms of epithelia, where the centrosomes lie in the outer end of the cell, often very near the surface.[1] (Fig. 23)

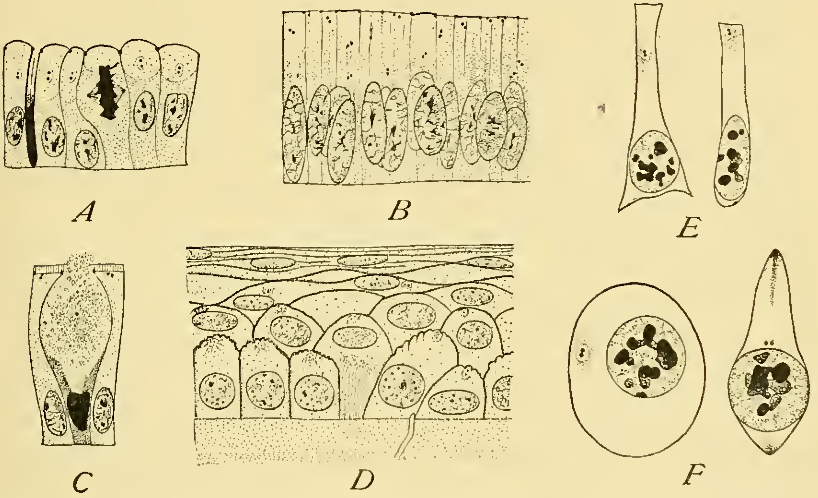

Fig. 23. — Centrosomes in epithelial and other cells. [*A*, *D*, Zimmermann; *E*, Heidenhain and Cohn; *F*, Heidenhain.]

A. From gastric glands of man; dead cell at the left. *B*. Uterine epithelium, man. *C*. From human duodenum; goblet-cell, with centrosome in the middle. *D*. Corneal epithelium of monkey. *E*. Epithelial cells from mesoblast-somites, embryo duck. *F*. Red blood-corpuscles from the duck-embryo. The centrosomes are double in nearly all cases.

and the recent observations of Henneguy ('98) and Lenhossék ('98, 1) give reason to believe that the "basal bodies" to which the cilia of ciliated epithelium are attached may be the centrosomes.[2] These facts are of very high significance; for the position of the centrosome, and hence the direction of the axis, is here obviously related to the cell-environment, and it is difficult to avoid the conclusion that the latter must be the determining condition to which the intracellular relations conform. When applied to the germ-cells, this conclusion becomes of high interest; for the polarity of the egg is one of the primary conditions of development, and we have here, as I believe, a clue to its determination.[1]

---

[1] Zimmermann, '98; Heidenhain and Cohn, '97.

[2] *Cf.* p. 356.

I. The Cell in Relation to the Multicellular Body

In analyzing the structure and functions of the individual cell we are accustomed, as a matter of convenience, to regard it as an independent elementary organism or organic unit. Actually, however, it is such an organism only in the case of the unicellular plants and animals and the germ-cells of the multicellular forms. When we consider the tissue-cells of the latter, we must take a somewhat different view. As far as structure and origin are concerned the tissue-cell is unquestionably of the same morphological value as the one-celled plant or animal; and *in this sense* the multicellular body is equivalent to a colony or aggregate of one-celled forms. Physiologically, however, the tissue-cell can only in a limited sense be regarded as an independent unit; for its autonomy is merged in a greater or less degree into the general life of the organism. From this point of view the tissue-cell must in fact be treated as merely a localized area of activity, provided it is true with the complete apparatus of cell-life, and even capable of independent action within certain limits, yet nevertheless a part and not a whole.

There is at present no biological question of greater moment than the means by which the individual cell-activities are coördinated, and the organic unity of the body maintained; for upon this question hangs not only the problem of the transmission of acquired characters, and the nature of development, but our conception of life itself. Schwann, the father of the cell-theory, very clearly perceived this; and after an admirably lucid discussion of the facts known to him ('39), drew the conclusion that the life of the organism is essentially a composite; that each cell has its independent life; and that "the whole organism subsists only by means of the reciprocal action of the single elementary parts."[2] This conclusion, afterward elaborated by Virchow and Haeckel to the theory of the "cell-state," took a very strong hold on the minds of biological investigators, and is even now widely accepted. It is, however, becoming more and more clearly apparent that this conception expresses only a part of the truth, and that Schwann went too far in denying the influence of the totality of the organism upon the local activities of the cells. It would of course be absurd to maintain that the whole can consist of more than the sum of its parts. Yet, as far as growth and development are concerned, it has now been clearly demonstrated that only in a limited sense can the cells be regarded as coöperating units. They are rather local centres of a formative power pervading the growing mass as a whole,[1] and the physiological autonomy of the individual cell falls into the background. It is true that the cells may acquire a high degree of physiological independence in the later stages of embryological development. The facts to be discussed in the eighth and ninth chapters will, however, show strong reason for the conclusion that this is a secondary result of development, through which the cells become, as it were, emancipated in a greater or less degree from the general control. Broadly viewed, therefore, the life of the multicellular organism is to be conceived as a whole; and the apparently composite character which it may exhibit is owing to a secondary distribution of its energies among local centres of action.[2]

---

[1] *Cf.* pp. 384, 424. We should remember that the germ-cells are themselves epithelial products.

[2] *Untersuchungen*, Trans., p. 181.

In this light the structural relations of tissue-cells become a question of great interest; for we have here to seek the means by which the individual cell comes into relation with the totality of the organism, and by which the general equilibrium of the body is maintained. It must be confessed that the results of microscopical research have not thus far given a very certain answer to this question. Though the tissue-cells are often apparently separated from one another by a non-living intercellular substance, which may appear in the form of solid walls, it is by no means certain that their organic continuity is thus actually severed. Many cases are known in which division of the nucleus is not followed by division of the cell-body, so that multinuclear cells or *syncytia* are thus formed, consisting of a continuous mass of protoplasm through which the nuclei are scattered. Heitzmann long since contended ('73), though on insufficient evidence, that division is incomplete in nearly all forms of tissue, and that even when cell-walls are formed they are traversed by strands of protoplasm by means of which the cell-bodies remain in organic continuity. The whole body was thus conceived by him as a syncytium, the cells being no more than nodal points in a general reticulum, and the body forming a continuous protoplasmic mass.

This interesting view, long received with scepticism, has been to a considerable extent sustained by later researches, and though it still remains *sub judice*, has been definitely accepted in its entirety by some recent workers. The existence of protoplasmic cell-bridges between the sieve-tubes of plants has long been known; and Tangl's discovery, in 1879, of similar connections between the endosperm-cells was followed by the demonstration by Gardiner, Kienitz-Gerloff, A. Meyer, and many others, that in nearly all plant-tissues the cell-walls are traversed by delicate intercellular bridges. Similar bridges have been conclusively demonstrated by Ranvier, Bizzozero, Retzius, Flemming, Pfitzner, and many later observers in nearly all forms of epithelium (Fig. 1); and they are asserted to occur in the smooth muscle-fibres, in cartilage-cells and connective tissue-cells, and in some nerve-cells. Dendy ('88), Paladino ('90), and Retzius ('89) have endeavoured to show, further, that the follicle-cells of the ovary are connected by protoplasmic bridges not only with one another, *but also with the ovum;* and similar protoplasmic bridges between germ-cells and somatic cells have been also demonstrated in a number of plants, *e.g.* by Goroschankin ('83) and Ikeno ('98) in the cycads and by A. Meyer ('96) in *Volvox.* On the strength of these observations some recent writers have not hesitated to accept the probability of Heitzmann's original conception, A. Meyer, for example, expressing the opinion that both the plant and the animal individual are continuous masses of protoplasm, in which the cytoplasmic substance forms a morphological unit, whether in the form of a single cell, a multinucleated cell, or a system of cells.[1] Captivating as this hypothesis is, its full acceptance at present would certainly be premature; and as far as adult animal tissues are concerned, it still remains undetermined how far the cells are in direct protoplasmic continuity. It is obvious that no such continuity exists in the case of the corpuscles of blood and lymph and the wandering leucocytes and pigment-cells. In case of the nervous system, which from an *a priori* point of view would seem to be above all others that in which protoplasmic continuity is to be expected, its occurrence and significance are still a subject of debate. When, however, we turn to the embryonic stages we find strong reason for the belief that a material continuity between cells here exists. This is certainly the case in the early stages of many arthropods, where the whole embryo is at first an unmistakable syncytium; and Adam Sedgwick has endeavoured to show that in *Peripatus* and even in the vertebrates the entire embryonic body, up to a late stage, is a continuous syncytium. I have pointed out ('93) that even in a total cleavage, such as that of *Amphioxus* or the echinoderms, the results of experiment on the early stages of cleavage are difficult to explain, save under the assumption that there must be a structural continuity from cell to cell that is broken by mechanical displacement of the blastomeres. This conclusion is supported by the recent work of Hammar ('96, '97), whose observations on sea-urchin eggs I can in the main confirm.

---

[1] *Cf.* Chapters VIII., IX.

[2] For a fuller discussion see pp. 388 and 413.

Among the most interesting observations in this direction are those of Mrs. Andrews ('97),[2] who asserts that during the cleavage of the echinoderm-egg the blastomeres "spin" delicate protoplasmic filaments, by which direct protoplasmic continuity is established between them subsequent to each division. These observations, if correct, are of high importance; for if protoplasmic connections may be broken and re-formed at will, as it were, the adverse evidence of the blood-corpuscles and wandering cells loses much of its weight. Meyer ('96) adduces evidence that in *Volvox* the cell-bridges are formed anew after division; and Flemming has also shown that when leucocytes creep about among epithelial cells they rupture the protoplasmic bridges, which are then formed anew behind them.[1]

---

[1] '96, p. 212. *Cf.* also the views of Hanstein, Strasburger, Russow, and others there cited.

[2] *Cf.* also E. A. Andrews, '98, 1, '98, 2.

We are still almost wholly ignorant of the precise physiological meaning of the cell-bridges; but the facts indicate that they are not merely channels of nutrition, as some authors have maintained, but paths of subtler physiological impulse. Beside the facts determined by the isolation of blastomeres, referred to above, may be placed Townsend's recent remarkable experiments on plants, described at page 346. If correct, these experiments give clear evidence of the transference of physiological influences from cell to cell by means of protoplasmic bridges, showing that the nucleus of one cell may thus control the membrane-forming activity in an enucleated fragment of another cell. The field of research opened up by these and related researches seems one of the most promising in view; but until it has been more fully explored, judgment should be reserved regarding the whole question of the occurrence, origin, and physiological meaning of the protoplasmic cell-bridges.

LITERATURE. I[2]

Altmann, R. — Die Elementarorganismen und ihre Beziehungen zu den Zellen, 2d ed. *Leipzig*, 1894.

L'Année Biologique. — *Paris*, 1895–96. (Full Reviews and Literature-lists.)

Böhm and Davidoff. — Lehrbuch der Histologie des Menschen. *Wiesbaden*, 1895.

Boveri, Th. — (See Lists IV., V.)

Bütschli, O. — Untersuchungen über mikroskopische Schäume und das Protoplasma. *Leipzig* (Engelmann), 1892.

Id. — Untersuchungen über Struktur. *Leipzig*, 1898.

Carnoy, J. B. — La Biologie Cellulaire. *Lierre*, 1884.

Engelmann, T. W. — Zur Anatomie und Physiologie der Flimmerzellen: *Arch. ges. Phys.*, XXIII. 1880.

Erlanger, R. v. Neuere Ansichten über die Struktur des Protoplasmas: *Zool. Centralbl.*, III. 8, 9. 1896.

Fischer, A. Fixierung, Färbung und Bau des Protoplasmas. *Jena*, 1899.

Flemming, W. Zellsubstanz, Kern und Zellteilung. *Leipzig*, 1882.

Id. Zelle: *Merkel und Bonnet's Ergebnisse*, I.–VII. 1891–97. (Admirable reviews and literature-lists.)

[1] '95, pp. 10–11; '97, p. 261.

[2] See also Introductory list, p. 14.

Heidenhain, M. — Über Kern und Protoplasma: *Festschr. z. 50-jähr. Doctorjub. von v. Kölliker. Leipzig*, 1893.

Klein, E. — Observations on the Structure of Cells and Nuclei: *Quart. Journ. Mic. Sci.*, XVIII. 1878.

Kölliker, A. — Handbuch der Gewebelehre, 6th ed. *Leipzig*, 1889.

Leydig, Fr. — Zelle und Gewebe. *Bonn*, 1885.

Schäfer, E. A. — General Anatomy or Histology; in *Quain's Anatomy*, I., 2. 10th ed. *London*, 1891.

Schiefferdecker & Kossel. — Die Gewebe des Menschlichen Körpers. *Braunschweig*, 1891.

Schwarz, Fr. — Die morphologische und chemische Zusammensetzung des Protoplasmas. *Breslau*, 1887.

Strasburger, E. — Zellbildung und Zellteilung, 3d ed. 1880.

Id. — Das Botanische Practicum, 3d ed. *Jena*, 1897.

Strasburger, Noll, Schenck, and Schimper. — Lehrbuch der Botanik, 3d ed. *Jena*, 1897.

Stricker, S. — Handbuch der Lehre von den Geweben. *Leipzig*, 1871.

Thoma, R. — Text-book of General Pathology and Pathological Anatomy: trans. by Alex. Bruce. *London*, 1896.

Van Beneden, E. — (See Lists II., IV.)

De Vries, H. — Intracellulare Pangenesis. *Jena*, 1889.

Waldeyer, W. — Die neueren Ansichten über den Bau und das Wesen der Zelle: *Deutsch. Med. Wochenschr.*, Oct., Nov., 1895.

Wiesner, J. — Die Elementarstruktur u. das Wachstum der lebenden Substanz: *Wien, Hölder*. 1892.

Wilson, E. B. — The Structure of Protoplasm: *Journ. Morph.*, XV. Suppl.; also *Wood's Holl Biol. Lectures*, 1899.

Zimmermann, A. — Beiträge zur Morphologie und Physiologie der Pflanzenzelle. *Tübingen*, 1893.

Id. — Die Morphologie und Physiologie des Pflanzlichen Zellkernes. *Jena*, 1896.

CHAPTER II

CELL-DIVISION

> "Wo eine Zelle entsteht, da muss eine Zelle vorausgegangen sein, ebenso wie das Thier nur aus dem Thiere, die Pflanze nur aus der Pflanze entstehen kann. Auf diese Weise ist, wenngleich es einzelne Punkte im Körper gibt, wo der strenge Nachweis noch nicht geliefert ist, doch das Princip gesichert, dass in der ganzen Reihe alles Lebendigen, dies mögen nun ganze Pflanzen oder thierische Organismen oder integrirende Theile derselben sein, ein ewiges Gesetz der *continuirlichen Entwicklung* besteht." VIRCHOW.[1]

THE law of genetic cellular continuity, first clearly stated by Virchow in the above words, has now become one of the primary data of biology, and the advance of research is ever adding weight to the conclusion that the cell has no other mode of origin than by division of a preëxisting cell. In the multicellular organism all the tissue-cells arise by continued division from the original germ-cell, and this in its turn arises by the division of a cell preëxisting in the parent-body. By *cell-division*, accordingly, the hereditary substance is split off from the parent-body; and by cell-division, again, this substance is handed on by the fertilized egg-cell or oösperm to every part of the body arising from it.[2] Cell-division is, therefore, one of the central facts of development and inheritance.

The first two decades after Schleiden and Schwann ('40–'60) were occupied with researches, on the part both of botanists and of zoölogists, which finally demonstrated the universality of this process and showed the authors of the cell-theory to have been in error in asserting the independent origin of cells out of a formative blastema.[3] The mechanism of cell-division was not precisely investigated until long afterward, but the researches of Remak ('41), Kölliker ('44), and others showed that an essential part of the process is a division of both the nucleus and the cell-body. In 1855 (*l.c.*, pp. 174, 175), and again in 1858, Remak gave as the general result of his researches the following synopsis or scheme of cell-division. Cell-division, he asserted, proceeds from the centre toward the periphery. It begins with the division of the nucleolus, is continued by simple constriction and division of the nucleus, and is completed by division of the cell-body and membrane (Fig. 24). For many years this account was accepted, and no essential advance beyond Remak's scheme was made for nearly twenty years. A number of isolated observations were, however, from time to time made, even at a very early period, which seemed to show that cell-division was by no means so simple an operation as Remak believed. In some cases the nucleus seemed to disappear entirely before cell-division (the germinal vesicle of the ovum, according to Reichert, Von Baer, Robin, etc.); in others to become lobed or star-shaped, as described by Virchow and by Remak himself (Fig. 24, *f*). It was not until 1873 that the way was opened for a better understanding of the matter. In this year the discoveries of Anton Schneider, quickly followed by others in the same direction by Bütschli, Fol, Strasburger, Van Beneden, Flemming, and Hertwig, showed cell-division to be a far more elaborate process than had been supposed, and to involve a complicated transformation of the nucleus to which Schleicher ('78) afterward gave the name of *karyokinesis*. It soon appeared, however, that this mode of division was not of universal occurrence; and that cell-division is of two widely different types, which Van Beneden ('76) distinguished as *fragmentation*, corresponding nearly to the simple process described by Remak, and *division*, involving the more complicated process of karyokinesis. Three years later Flemming ('79) proposed to substitute for these the terms *direct* and *indirect* division, which are still used. Still later ('82) the same author suggested the terms *mitosis* (indirect or karyokinetic division) and *amitosis* (direct or akinetic division), which have rapidly made their way into general use, though the earlier terms are often employed.

---

[1] *Cellularpathologie*, p. 25, 1858.

[2] *Cf.* Introduction, p. 10.

[3] For a full historical account of this period, see Remak, *Untersuchungen über die Entwicklung der Wirbelthiere*, 1855, pp. 164–180. Also Tyson on the *Cell-doctrine* and Sachs's *Geschichte der Botanik.*

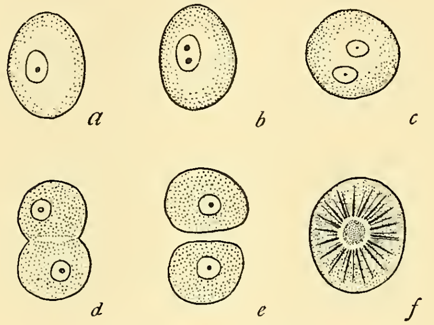

Fig. 24. — Direct division of blood-cells in the embryo chick, illustrating Remak's scheme. [REMAK.]

a–e. Successive stages of division; *f.* cell dividing by mitosis.

Modern research has demonstrated the fact that amitosis or direct division, regarded by Remak and his immediate followers as of universal occurrence, is in reality a rare and exceptional process; and there is reason to believe, furthermore, that it is especially characteristic of highly specialized cells incapable of long-continued multiplication or such as are in the early stages of degeneration, for instance, in glandular epithelia and in the cells of transitory embryonic envelopes, where it is of frequent occurrence. Whether this view be well founded or not, it is certain that in all the higher and in many of the lower forms of life, indirect division or mitosis is the typical mode of cell-division. It is by mitotic division that the germ-cells arise and are prepared for their union during the process of maturation, and by the same process the oösperm segments and gives rise to the tissue-cells. It occurs not only in the highest forms of plants and animals, but also in such simple forms as the rhizopods, flagellates, and diatoms. We may, therefore, justly regard it as the most general expression of the "eternal law of continuous development" on which Virchow insisted.

A. OUTLINE OF INDIRECT DIVISION OR MITOSIS (KARYOKINESIS)

In the present state of knowledge it is somewhat difficult to give a connected general account of mitosis, owing to the uncertainty that hangs over the nature and functions of the centrosome. For the purpose of the following preliminary outline, we shall take as a type mitosis in which a distinct and persistent centrosome is present, as has been most clearly determined in the maturation and cleavage of various animal eggs, and in the division of the testis-cells. In such cases the process involves three parallel series of changes, which affect the nucleus, the centrosome, and the cytoplasm of the cell-body respectively. For descriptive purposes it may conveniently be divided into a series of successive stages or phases, which, however, graduate into one another and are separated by no well-defined limits. These are: (1) The *Prophases*, or preparatory changes; (2) the *Metaphase*, which involves the most essential step in the division of the nucleus; (3) the *Anaphases*, in which the nuclear material is distributed; (4) the *Telophases*, in which the entire cell divides and the daughter-cells are formed.

1. *Prophases.* — (*a*) *The Nucleus.* As the cell prepares for division, the most conspicuous fact is a transformation of the nuclear substance, involving both physical and chemical changes. The chromatin-substance rapidly increases in staining-power, loses its net-like arrangement, and finally gives rise to a definite number of separate intensely staining bodies, usually rod-shaped, known as *chromosomes.* As a rule this process, exemplified by the dividing cells of the salamander-epidermis (Fig. 1) or those of plant-meristem (Fig. 2), takes place as follows. The chromatin resolves itself little by little into a more or less convoluted thread, known as the *skein* (Knäuel) or *spireme*, and its substance stains far more intensely than that of the reticulum (Fig. 25). The spireme-thread is at first fine and closely convoluted, forming the "close spireme." Later the thread thickens and shortens and the

convolution becomes more open ("open spireme"). In some cases there is but a single continuous thread; in others, the thread is from

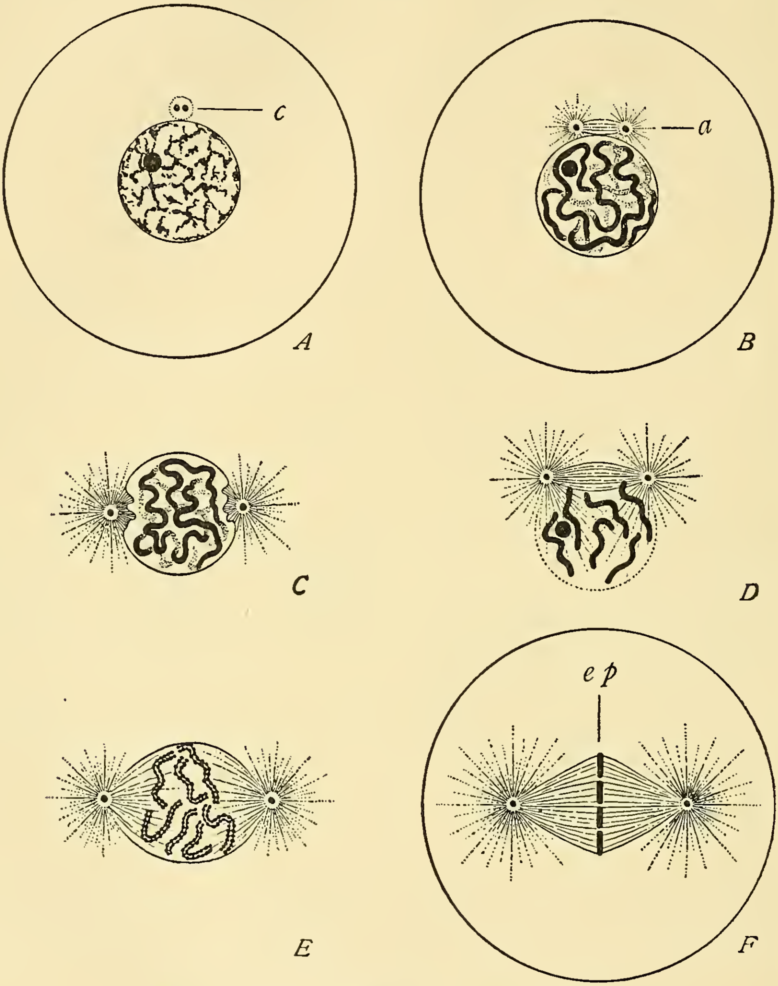

Fig. 25. — Diagrams showing the prophases of mitosis.

A. Resting cell with reticular nucleus and true nucleolus; at *c* the attraction-sphere containing two centrosomes. *B.* Early prophase; the chromatin forming a continuous *spireme*, nucleolus still present; above, the amphiaster (*a*). *C. D.* Two different types of later prophases. *C.* Disappearance of the primary spindle, divergence of the centrosomes to opposite poles of the nucleus (examples, some plant-cells, cleavage-stages of many eggs). *D.* Persistence of the primary spindle (to form in some cases the "central spindle"), fading of the nuclear membrane, ingrowth of the astral rays, segmentation of the spireme-thread to form the chromosomes (examples, epidermal cells of salamander, formation of the polar bodies). *E.* Later prophase of type *C*; fading of the nuclear membrane at the poles, formation of a new spindle inside the nucleus; precocious splitting of the chromosomes (the latter not characteristic of this type alone). *F.* The mitotic figure established; *e.p.* the equatorial plate of chromosomes. (*Cf.* Figs. 21, 27, 32, etc.)

its first appearance divided into a number of separate pieces or segments, forming a *segmented spireme.* In either case it ultimately breaks transversely to form the *chromosomes*, which in most cases have the form of rods, straight or curved, though they are sometimes spherical or ovoidal, and in certain cases may be joined together in the form of rings. The staining-power of the chromatin is now at a maximum. As a rule the nuclear membrane meanwhile fades away and finally disappears, though there are some cases in which it persists more or less completely through all the phases of division. The chromosomes now lie naked in the cell, and the ground-substance of the nucleus becomes continuous with the surrounding cytoplasm (Fig. 25, *D*, *E*, *F*).[1]

The remarkable fact has now been established with high probability that *every species of plant or animal has a fixed and characteristic number of chromosomes, which regularly recurs in the division of all of its cells ; and in all forms arising by sexual reproduction the number is even.* Thus, in some of the sharks the number is 36; in certain gasteropods it is 32 ; in the mouse, the salamander, the trout, the lily, 24 ; in the worm *Sagitta*, 18 ; in the ox, guinea-pig, and in man [2] the number is said to be 16, and the same number is characteristic of the onion. In the grasshopper it is 12 ; in the hepatic *Pallavicinia* and some of the nematodes, 8 ; and in *Ascaris*, another thread-worm, 4 or 2. In the crustacean *Artemia* it is 168.[3] Under certain conditions, it is true, the number of chromosomes may be less than the normal in a given species; but these variations are only apparent exceptions (p. 87). The even number of chromosomes is a most interesting fact, which, as will appear hereafter (p. 205), is due to the derivation of one-half the number from each of the parents.

The nucleoli differ in their behaviour in different cases. Net-knots, or chromatin-nucleoli, contribute to the formation of the chromosomes; and in cases such as *Spirogyra* (Meunier, '86, and Moll, '93) or *Actinosphærium* (R. Hertwig, '99), where the whole of the chromatin is at one period concentrated into a single mass, the whole chromatic figure thus appears to arise from a "nucleolus." True nucleoli or plasmosomes sooner or later disappear ; and the greater number of observers agree that they do not take part in the chromosome-formation. In a considerable number of forms (*e.g.* during the formation of the polar bodies in various eggs) the nucleolus is cast out into the cytoplasm as the spindle forms, to persist as a "metanucleus" for some time before its final disappearance (Fig. 104). More commonly the nucleolus fades away *in situ*, sometimes breaking into fragments meanwhile, while the chromosomes and spindle are forming. The fate of the material is in this case only conjectural. An interesting view is that of Strasburger ('95, '97), who suggests that the true nucleoli are to be regarded as storehouses of "kinoplasmic" material, which is either directly used in the formation of the spindle, or, upon being cast out of the nucleus, adds to the cytoplasmic store of "kinoplasm" available for future mitosis.

---

[1] The spireme-formation is by no means an invariable occurrence in mitosis. In a considerable number of cases the chromatin-network resolves itself directly into the chromosomes, the chromatic substance becoming concentrated in separate masses which never form a continuous thread. Such cases are connected by various gradations with the "segmented spireme."

[2] Flemming believes the number in man to be considerably greater than 16.

[3] For a more complete list see p. 206.

(*b*) *The Amphiaster.* Meanwhile, more or less nearly parallel with these changes in the chromatin, a complicated structure known as the *amphiaster* (Fol, '77) makes its appearance in the position formerly occupied by the nucleus (Fig. 25, *B–F*). This structure consists of a fibrous spindle-shaped body, the *spindle*, at either pole of which is a star or *aster* formed of rays or astral fibres radiating into the surrounding cytoplasm, the whole strongly suggesting the arrangement of iron filings in the field of a horseshoe magnet. The centre of each aster is occupied by a minute body, known as the *centrosome* (Boveri, '88), which may be surrounded by a spherical mass known as the *centrosphere* (Strasburger, '93). As the amphiaster forms, the chromosomes group themselves in a plane passing through the equator of the spindle, and thus form what is known as the *equatorial plate.*

The amphiaster arises under the influence of the centrosome of the resting cell, which divides into two similar halves, an aster being developed around each while a spindle stretches between them (Figs. 25, 27). In most cases this process begins outside the nucleus, but the subsequent phenomena vary considerably in different forms. In some forms (tissue-cells of the salamander) the amphiaster at first lies tangentially outside the nucleus, and as the nuclear membrane fades away, some of the astral rays grow into the nucleus from the side, become attached to the chromosomes, and finally pull them into position around the equator of the spindle, which is here called the *central spindle* (Figs. 25, *D, F;* 27). In other cases the original spindle disappears, and the two asters pass to opposite poles of the nucleus (some plant mitoses and in many animal-cells). A spindle is now formed from rays that grow into the nucleus from each aster, the nuclear membrane fading away at the poles, though in some cases it may be pushed in by the spindle-fibres for some distance before its disappearance (Figs. 25, 32). In this case there is apparently no central spindle. In a few exceptional cases, finally, the amphiaster may arise inside the nucleus (p. 304).

The entire structure, resulting from the foregoing changes, is known as the *karyokinetic* or *mitotic figure.* It may be described as consisting of two distinct parts; namely, 1, the *chromatic figure,* formed by the deeply staining chromosomes; and, 2, the *achromatic figure,* consisting of the spindle and asters which, in general, stain but slightly. The fibrous substance of the achromatic figure is generally known as *archoplasm* (Boveri, '88), but this term is not applied to the centrosome within the aster.

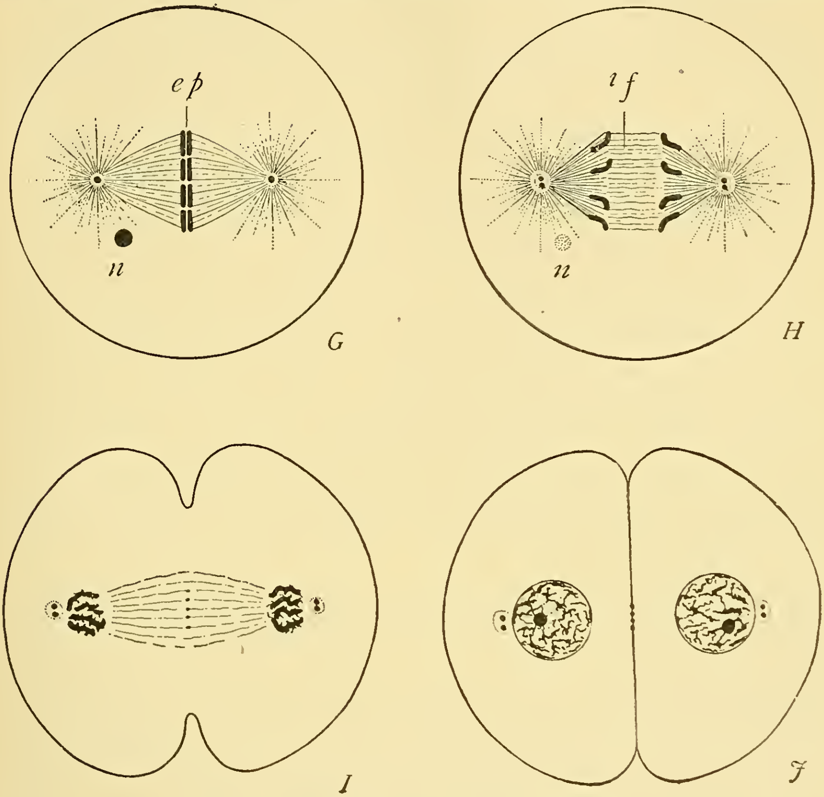

Fig. 26. — Diagrams of the later phases of mitosis.

G. Metaphase; splitting of the chromosomes (*e.p.*). *n.* The cast-off nucleolus. *H.* Anaphase; the daughter-chromosomes diverging, between them the interzonal-fibres (*i.f.*), or central spindle; centrosomes already doubled in anticipation of the ensuing division. *I.* Late anaphase or telophase, showing division of the cell-body, mid-body at the equator of the spindle and beginning reconstruction of the daughter-nuclei. *J.* Division completed.

2. *Metaphase.* — The *prophases* of mitosis are, on the whole, preparatory in character. The *metaphase*, which follows, forms the initial phase of actual division. Each chromosome splits lengthwise into two exactly similar halves, which afterward diverge to opposite poles of the spindle, and here each group of daughter-chromosomes

finally gives rise to a daughter-nucleus (Fig. 26). In some cases the splitting of the chromosomes cannot be seen until they have grouped themselves in the equatorial plane of the spindle; and it is only in this case that the term "metaphase" can be applied to the mitotic figure as a whole. In a large number of cases, however, the splitting may take place at an earlier period in the spireme-stage, or even, in a few cases, in the reticulum of the mother-nucleus (Figs. 54, 55). Such variations do not, however, affect the essential fact that *the chromatic network is converted into a thread*[1] *which, whether continuous or discontinuous, splits throughout its entire length into two exactly equivalent halves.* The splitting of the chromosomes, discovered by Flemming in 1880, is the most significant and fundamental operation of cell-division; for by it, as Roux first pointed out ('83), the entire substance of the chromatic network is precisely halved, and *the daughter-nuclei receive precisely equivalent portions of chromatin from the mother-nucleus.* It is very important to observe that the *nuclear* division always shows this exact quality, whether division of the cell-body be equal or unequal. The minute polar body, for example (p. 238), receives exactly the same amount of chromatin as the egg, though the latter is of gigantic size as compared with the former. On the other hand, the size of the asters varies with that of the daughter-cells (Figs. 58, 175), though not in strict ratio. The fact is one of great significance for the general theory of mitosis, as will appear beyond.

3. *Anaphases.* — After splitting of the chromosomes, the daughter-chromosomes, arranged in two corresponding groups,[2] diverge to opposite poles of the spindle, where they become closely crowded in a mass near the centre of the aster. As they diverge, the two groups of daughter-chromosomes are connected by a bundle of achromatic fibres, stretching across the interval between them, and known as the *interzonal fibres* or *connecting fibres.*[3] In some cases these differ in a marked degree from the other spindle-fibres; and they are believed by many observers to have an entirely different origin and function. A view now widely held is that of Hermann, who regards these fibres as belonging to a *central spindle*, surrounded by a peripheral layer of *mantle-fibres* to which the chromosomes are attached, and only exposed to view as the chromosomes separate.[4] Almost invariably in the division of plant-cells and often in that of animal cells these

---

[1] It was this fact that led Flemming to employ the word *mitosis* (μίτος, a thread).

[2] This stage is termed by Flemming the *dyaster*, a term which should, however, be abandoned in order to avoid confusion with the earlier word *amphiaster.* The latter convenient and appropriate term clearly has priority.

[3] *Verbindungsfasern* of German authors; *filaments réunissants* of Van Beneden.

[4] *Cf.* p. 105.

fibres show during this period a series of deeply staining thickenings in the equatorial plane forming the *cell-plate* or *mid-body*. In plant-mitoses this is a very conspicuous structure (Fig. 34). In animal cells the mid-body is usually less developed and sometimes rudimentary, being represented by only a few granules or even a single one (Fig. 29). Its later history is described below.

4. *Telophases.* — In the final phases of mitosis, the entire cell divides in two in a plane passing through the equator of the spindle, each of the daughter-cells receiving a group of chromosomes, half of the spindle, and one of the asters with its centrosome. Meanwhile, a daughter-nucleus is reconstructed in each cell from the group of chromosomes it contains. The nature of this process differs greatly in different kinds of cells. Sometimes, as in the epithelial cells of Amphibia, especially studied by Flemming and Rabl, and in many plant-cells, the daughter-chromosomes become thickened, contorted, and closely crowded to form a *daughter-spireme*, closely similar to that of the mother-nucleus (Fig. 29); this becomes surrounded by a membrane, the threads give forth branches, and thus produce a reticular nucleus. A somewhat similar set of changes takes place in the segmenting eggs of *Ascaris* (Van Beneden, Boveri). In other cases, as in many segmenting ova, each chromosome gives rise to a hollow vesicle, after which the vesicles fuse together to produce a single nucleus (Fig. 52). When first formed, the daughter-nuclei are of equal size. If, however, division of the cell-body has been unequal, the nuclei become, in the end, correspondingly unequal — a fact which, as Conklin and others have pointed out, proves that the size of the nucleus is controlled by that of the cytoplasmic mass in which it lies.

The fate of the achromatic structures varies considerably, and has been accurately determined in only a few cases. As a rule, the spindle-fibres disappear more or less completely, but a portion of their substance sometimes persists in a modified form (*e.g.* the *Nebenkern*, p. 163). In dividing plant-cells, the cell-plate finally extends across the entire cell and splits into two layers, between which appears the membrane by which the daughter-cells are cut apart.[1] A nearly similar process occurs in a few animal cells,[2] but as a rule the cell-plate is here greatly reduced and forms no membrane, the cell dividing by constriction through the equatorial plane. Even in this case, however, the division-plane is often indicated before division takes place by a peculiar modification of the cytoplasm in the equatorial plane outside the spindle (Fig. 30). This region is sometimes called the *cytoplasmic plate*, in contradistinction to the *spindle-plate*, or mid-body proper. In the prophases and metaphases the astral rays often cross one another in the equatorial region outside the spindle. During the anaphases, however, this crossing disappears, the rays from the two asters now meeting at an angle along the cytoplasmic plate (Fig. 31). Constriction and division of the cell then occur.[1]

---

[1] *Cf.* Strasburger, '98.

[2] *Cf.* Hoffmann, '98.

The aster may in some cases entirely disappear, together with the centrosome (as occurs in the mature egg). In a large number of cases, however, the centrosome persists, lying either outside or more rarely inside the nucleus and dividing into two at a very early period. This division is clearly a precocious preparation for the ensuing division of the daughter-cell, and it is a remarkable fact that it occurs as a rule during the early anaphase, before the mother-cell itself has divided. There are apparently, however, some cases in which the centrosome remains undivided during the resting stage and only divides as the process of mitosis begins.

Like the centrosome, the aster or its central portion may persist in a more or less modified form throughout the resting state of the cell, forming a structure generally known as the *attraction-sphere*. This body often shows a true astral structure with radiating fibres (Figs. 8, 49); but it is sometimes reduced to a regular spherical mass which may represent only a portion of the original aster (Fig. 7).

B. Origin of the Mitotic Figure

The nature and source of the material from which the mitotic figure arises form a problem that has been almost continuously under discussion since the first discovery of mitosis, and is even now but partially solved. The discussion relates, however, almost solely to the achromatic figure (centrosome, spindle, and asters); for every one is agreed that the chromatic figure (chromosomes) is directly derived from the chromatin-network, as described above, so that there is no breach in the continuity of the chromatin from one cell-generation to another. With the achromatic figure the case is widely different. The material of the spindle and asters must be derived from the nucleus, from the cytoplasm, or from both; and most of the earlier research was devoted to an endeavour to decide between these possibilities. The earliest observers ('73–'75) supposed the achromatic figure to disappear entirely at the close of cell-division, and most of them (Bütschli, Strasburger, Van Beneden, '75) believed it to be re-formed at each succeeding division out of the nuclear substance. The entire mitotic figure was thus conceived as a metamorphosed nucleus. Later researches ('75–'85) gave contradictory and apparently irreconcilable results. Fol ('79) derived the spindle from the nuclear material, the asters from the cytoplasm. Strasburger ('80) asserted that the entire achromatic figure arose

---

[1] See p. 318. *Cf.* Kostanecki, '97, and Hoffmann, '98.

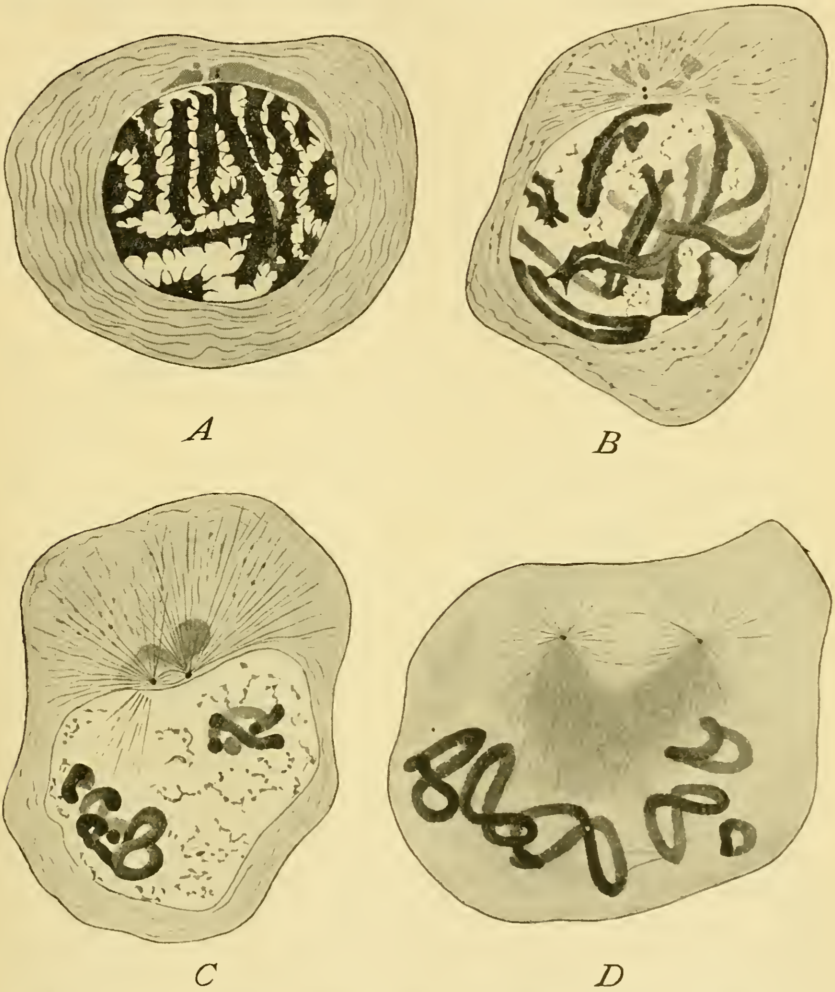

Fig. 27. — The prophases of mitosis (heterotypical form) in primary spermatocytes of *Salamandra*. [Meves.]

A. Early segmented spireme; two centrosomes outside the nucleus in the remains of the attraction-sphere. *B*. Longitudinal splitting of the spireme, appearance of the astral rays, disintegration of the sphere. *C*. Early amphiaster and central spindle. *D*. Chromosomes in the form of rings, nuclear membrane disappeared, amphiaster enlarging, mantle-fibres developing.

from the cytoplasm, and to that view, in a modified form, he still adheres. Flemming ('82), on the whole, inclined to the opinion that the achromatic figure arose inside the nucleus, yet expressed the opinion that the question of nuclear or cytoplasmic origin was one of minor importance. A long series of later researches on both plants and animals has fully sustained this opinion, showing that the origin of the achromatic figure does in fact differ in different cases. Thus in Infusoria the entire mitotic figure is of intranuclear origin (there are, however, no asters); in echinoderm eggs the spindle is of nuclear, the asters of cytoplasmic, origin; in the testis-cells and some tissue-cells of the salamander, a complete amphiaster is first formed in the cytoplasm, but to this are afterward added elements probably derived from the linin-network; while in higher plants there is some reason to believe that the entire achromatic figure may be of cytoplasmic origin. Such differences need not surprise us when we reflect that the achromatic part of the nucleus (linin-network, etc.) is probably of the same general nature as the cytoplasm.[1]

Many observers have maintained that the material of the astral rays and spindle-fibres is directly derived from the substance of the protoplasmic meshwork, whether nuclear, cytoplasmic, or both; but its precise origin has long been a subject of debate. This question, critically considered in Chapter VI., will be here only briefly sketched. By Klein ('78), Van Beneden ('83), Carnoy ('84, '85), and a large number of later observers, the achromatic fibres, both of spindles and of asters, are regarded as identical with those of a preëxisting reticulum which have merely assumed a radiating arrangement about the centrosome. The amphiaster has, therefore, no independent existence, but is merely an image, as it were, somewhat like the bipolar figure arising when iron filings are strewn in the field of a horseshoe magnet. Boveri, on the other hand, who has a small but increasing following, maintains that the amphiastral fibres are not identical with those of the preëxisting meshwork, but a new formation which, as it were, "crystallizes anew" out of the general protoplasmic substance. The amphiaster is therefore a new and independent structure, arising in, or indirectly from, the preëxisting material, but not by a *direct* morphological transformation of that material. This view, which has been advocated by Drüner ('94), Braus ('95), Meves ('97, 4, '98), and with which my own later observations ('99) also agree, is more fully discussed at page 318.

In 1887 an important forward step was taken through the independent discovery by Van Beneden and Boveri that in the egg of *Ascaris* the centrosome does not disappear at the close of mitosis, but remains as a distinct cell-organ lying beside the nucleus in the cytoplasm. These investigators agreed that the amphiaster is formed under the influence of the centrosome, which by its division creates two new "centres of attraction" about which the astral systems arise, and which form the foci of the entire dividing system. In them are centred the fibrillæ of the astral system, toward them the daughter-chromosomes proceed, and within their respective spheres of influence are formed the resulting daughter-cells. Both Van Beneden and Boveri fully recognized the importance of their discovery. "We are justified," said Van Beneden, "in regarding the attraction-sphere with its central corpuscle as forming a permanent organ, not only of the early blastomeres, but of all cells, and as constituting a cell-organ equal

---

[1] In the case of echinoderm eggs, I have found reason ('95, 2) for the conclusion that the spindle-fibres are derived not merely from the linin-substance, but also from the chromatin. Despite some adverse criticism, I have found no reason to change my opinion on this point. The possible significance of such a derivation is indicated elsewhere (p. 302).

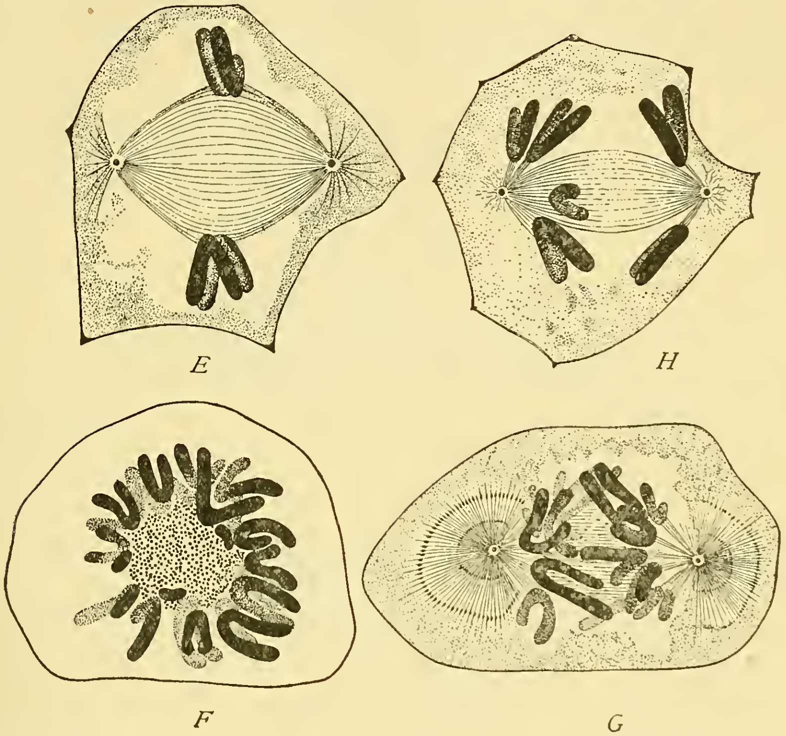

Fig. 28. — Metaphase and anaphases of mitosis in cells (spermatocytes) of the salamander. [Drüner.]

E. Metaphase. The continuous central spindle-fibres pass from pole to pole of the spindle. Outside them the thin layer of contractile mantle-fibres attached to the divided chromosomes, of which only two are shown. Centrosomes and asters. *F.* Transverse section through the mitotic figure showing the ring of chromosomes surrounding the central spindle, the cut fibres of the latter appearing as dots. *G.* Anaphase; divergence of the daughter-chromosomes, exposing the central spindle as the interzonal fibres; contractile fibres (principal cones of Van Beneden) clearly shown. *H.* Later anaphase (dyaster of Flemming); the central spindle fully exposed to view; mantle-fibres attached to the chromosomes. Immediately afterward the cell divides (see Fig. 29).

in rank to the nucleus itself; and we may conclude that every central corpuscle is derived from a preëxisting corpuscle, every attraction-sphere from a preëxisting sphere, and that division of the sphere precedes that of the cell-nucleus."[1] Boveri expressed himself in similar terms regarding the centrosome in the same year ('87, 2, p. 153), and the same general result was reached by Vejdovsky nearly at the same time,[2] though it was less clearly formulated than by either Boveri or Van Beneden.

All these observers agreed, therefore, that the achromatic figure arose outside the nucleus, in the cytoplasm; that the primary impulse to cell-division was given, not by the nucleus, but by the centrosome, and that a new cell-organ had been discovered whose special office was to preside over cell-division. "The centrosome is an independent permanent cell-organ, which, exactly like the chromatic elements, is transmitted by division to the daughter-cells. *The centrosome represents the dynamic centre of cell.*"[3]

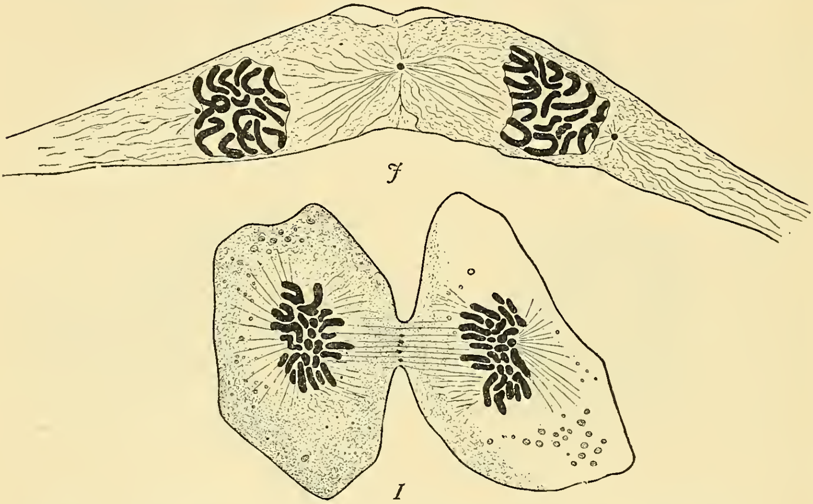

Fig. 29. — Final phases (telephases) of mitosis in salamander cells. [FLEMMING.]

I. Epithelial cell from the lung; chromosomes at the poles of the spindle, the cell-body dividing; granules of the "mid-body" or *Zwischenkörper* at the equator of the disappearing spindle. *J.* Connective tissue-cell (lung) immediately after division; daughter-nuclei reforming, the centrosome just outside of each; mid-body a single granule in the middle of the remains of the spindle.

That the centrosome does in many cases, especially in embryonic cells, behave in the manner stated by Van Beneden and Boveri seems at present to admit of no doubt; and it has been shown to occur in many kinds of adult tissue-cells during their resting state; for example in pigment-cells, leucocytes, connective tissue-cells, epithelial and endothelial cells, in certain gland-cells and nerve-cells, in the cells of some plant-tissues, and in some of the unicellular plants and animals, such as the diatoms and flagellates and rhizopods. On the other hand, Van Beneden's conception of the attraction-sphere has proved untenable; for this structure has been clearly shown in some cases to disintegrate and disappear at the close or the beginning of mitosis[1] (Fig. 27).

---

[1] '87, p. 279.

[2] '88, pp. 151, etc.

[3] Boveri, '87, 2, p. 153.

Whether the centrosome theory can be maintained is still in doubt; but evidence against it has of late rapidly accumulated.

In the first place, it has been shown that the primary impulse to cell-division cannot be given by fission of the centrosome, for there are several accurately determined cases in which the chromatin-elements divide independently of the centrosome, and it is now generally agreed that the division of chromatin and centrosome are two parallel events, the nexus between which still remains undetermined.[2]

Secondly, an increasing number of observers assert the total disappearance of the centrosome at the close of mitosis; while some very convincing observations have been made favouring the view that centrosomes may be formed *de novo* without connection with preëxisting ones (pp. 213, 305).

Thirdly, a large number of recent observers (including Strasburger and many of his pupils) of mitosis in the flowering plants and pteridophytes agree that in these forms *no centrosome exists at any stage of mitosis*, the centre of the aster being occupied by a vague reticular mass, and the entire achromatic figure arising by the gradual grouping of fibrous cytoplasmic elements (kinoplasm or filar plasm) about the nuclear elements.[3] If we can assume the correctness of these observations, the centrosome-theory must be greatly modified, and the origin of the amphiaster becomes a far more complex problem than it appeared under the hypothesis of Van Beneden and Boveri. That such is indeed the case is indicated by nothing more strongly than by Boveri's own remarkable recent experiments on cell-division (referred to at page 108).

C. Details of Mitosis

Comparative study has shown that almost every detail of the processes described above is subject to variation in different forms of cells. Before considering some of these modifications it may be well to point out what we are at present justified in regarding as its essential features. These are: (1) The formation of the chromatic and achromatic figures; (2) the longitudinal splitting of the chromosomes or spireme-thread; (3) the transportal of the chromatin-halves to the respective daughter-cells. Each of these three events is endlessly varied in detail; yet the essential phenomena are everywhere the same, with one important exception relating to the division of the chromosomes that occurs in the maturation of certain eggs and spermatozoa.[1] It may be stated further that the study of mitosis in some of the lower forms (Protozoa) gives reason to believe that the asters are of secondary importance as compared with the spindle, and that the formation of spireme and chromosomes is but tributary to the division of the smaller chromatin-masses of which they are made up.

---

[1] *Cf.* p. 323. [2] *Cf.* p. 108. [3] *Cf.* p. 82.

1. *Varieties of the Mitotic Figure*

(*a*) *The Achromatic Figure.* The phenomena involved in the history of the achromatic figure are in general most clearly displayed in embryonic or rapidly dividing cells, especially in egg-cells (Figs. 31, 60), where the asters attain an enormous development, and the centrosomes are especially distinct. In adult tissue-cells the asters are relatively small and difficult of demonstration, the spindle large and distinct; and this is particularly striking in the cells of higher plants where the asters are but imperfectly developed. Plant-mitoses are characterized by the prominence of the cell-plate (Fig. 34), which is rudimentary or often wanting in animals, a fact correlated no doubt with the greater development of the cell-membrane in plants. With this again is correlated the fact that division of the cell-body in animal cells generally takes place by constriction in the equatorial plane of the spindle; while in plant-cells the cell is usually cut in two by a cell-wall developed in the substance of the protoplasm and derived in large part from the cell-plate.

In animal cells we may distinguish two general types in the formation of the amphiaster, which are, however, connected by intermediate gradations. In the first of these, typically illustrated by the division of epithelial and testis-cells in the salamander (Flemming, Hermann, Drüner, Meves), a complete amphiaster is first formed in the cytoplasm outside the nucleus, while the nuclear membrane is still intact. As the latter fades away and the chromosomes appear, some of the astral rays grow into the nuclear space and become attached to the chromosomes, which finally arrange themselves in a ring about the original spindle (Figs. 27, 28). In the completed amphiaster, therefore, we may distinguish the original *central spindle* (Hermann, '91) from the surrounding *mantle-fibres*, the latter being attached to the chromosomes, and being, according to Hermann, the principal agents by which the daughter-chromosomes are dragged apart. The mantle-fibres thus form two hollow cones or half-spindles, separated at their bases by the chromosomes and completely surrounding the continuous fibres of the central spindle, which come into view as the "interzonal fibres" during the anaphases (Fig. 28).

---

[1] *Cf.* Chapter V.

There is still considerable uncertainty regarding the origin and relation of these two sets of fibres. It is now generally agreed with Van Beneden that the mantle-fibres are essentially a part of the asters, *i.e.* are simply those astral rays that come into connection with the chromosomes — wholly cytoplasmic in origin (Hermann, Drüner, MacFarland), or in part cytoplasmic, in part differentiated from the linin-network (Flemming, Meves). Drüner ('95), Braus ('95) (salamander), and MacFarland (*Pleurophyllidia*, '97) believe the central spindle to arise secondarily through the union of two opposing groups of astral rays in the area between the centrosomes. On the other hand, Hermann ('91), Flemming ('91), Heidenhain ('94), Kostanecki ('97), Van der Stricht ('98), and others believe the central spindle to exist from the first in the form of fibres stretching between the diverging centrosomes; and Heidenhain believes them to be developed from a special substance, forming a "primary centrodesmus," which persists in the resting cell, and in which the centrosomes are embedded.[1] MacFarland's observations on gasteropod-eggs ('97) indicate that even nearly related forms may differ in the origin of the central spindle, since in *Pleurophyllidia* it is of secondary origin, as described above, while in *Diaulula* it is a primary structure developed from what he describes as the "centrosome," but which, as shown at page 314, is probably to be regarded as

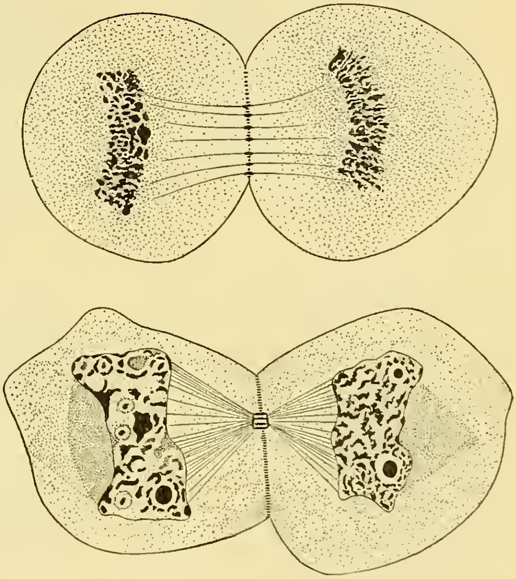

Fig. 30. — Mid-body in embryonic cells of *Limax*. [HOFFMANN.]

Earlier stage above, showing thickenings along the line of cleavage. Later stage, below, showing spindle-plate and cytoplasmic plate.

---

[1] *Cf.* p. 315.

an attraction-sphere surrounding the centrosomes, and is perhaps comparable to Heidenhain's "centrodesmus."

In the second type, illustrated in the cleavage of echinoderm, annelid, molluscan, and some other eggs, a central spindle may be formed, — sometimes already during the anaphases of the preceding mitosis (Figs. 99, 155), — but afterward disappears, the asters moving to opposite poles of the nucleus. Between these two poles a new spindle is then formed in the nuclear area, while astral rays grow out into the cytoplasm. There is strong evidence that in this case the entire spindle may arise inside the nucleus, *i.e.* from the substance of the linin-network, as occurs, for example, in the eggs of echinoderms (Fig. 25, *E*), and in the testis-cells of arthropods. In other cases, however, a part at least of the spindle is of cytoplasmic

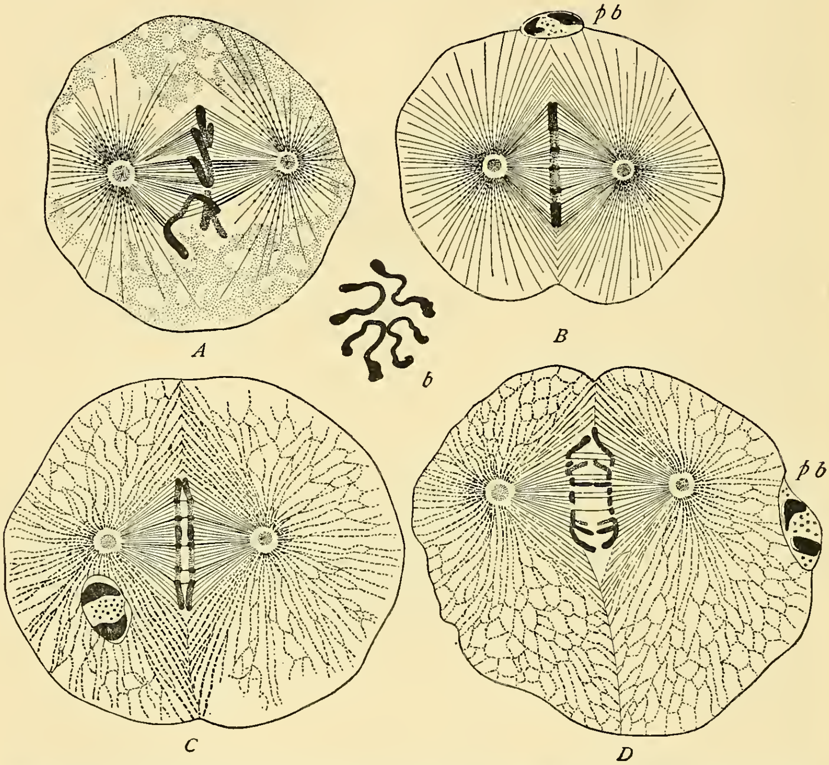

Fig. 31. — The middle phases ot mitosis in the first cleavage of the *Ascaris*-egg. [Boveri.]

A. Closing prophase, the equatorial plate forming. *B.* Metaphase; equatorial plate established and the chromosomes split; *b.* the equatorial plate, viewed *en face*, showing the four chromosomes. *C.* Early anaphase; divergence of the daughter-chromosomes (polar body at one side). *D.* Later anaphase; *p.b.* second polar body.

(For preceding stages see Fig. 90; for later stages Fig. 145.)

origin, since the ends of the spindle begin to form before dissolution of the nuclear membrane, and the latter is pushed inwards in folds by the ingrowing fibres (Figs. 25, *C*, 99).[1] In some cases, however, it seems certain that the nuclear membrane fades away before completion of the spindle (first maturation-division of *Thalassema*, *Chætopterus*), and it is probable that the middle region of the spindle is here formed from the linin-network. In most, if not all; mitoses of the second type the chromosomes do not form a ring about the equator of the spindle, but extend in a flat plate completely through its substance. Here, therefore, it is impossible to speak of a "central spindle." It is nevertheless probable that the spindle-fibres are of two kinds, viz. continuous fibres, which form the interzonal fibres seen during the anaphases, and half-spindle fibres, extending only from the poles to the chromosomes. It is possible that these two kinds of fibres, though having the same origin, respectively corre-

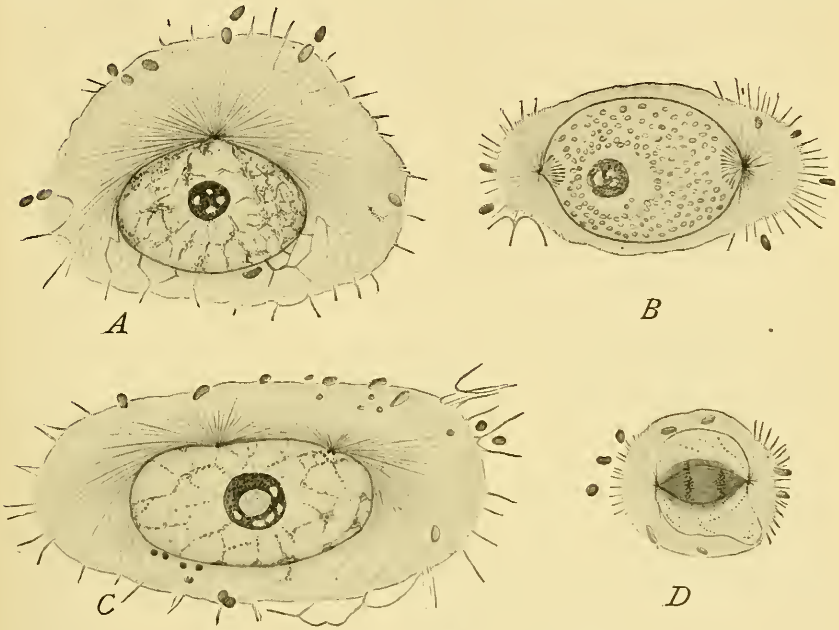

Fig. 32. — Mitosis in *Stypocaulon*. [SWINGLE.]

A. Early prophase with single aster and centrosome. *B*. Initial formation of intranuclear spindle. *C*. Divergence of the daughter-centrosomes. *D*. Early anaphase; nuclear membrane still intact.

---

[1] *Cf.* Platner ('86) on *Arion* and *Lepidoptera*, Watasé ('91) on *Loligo*, Braus ('95) on *Triton*, and Griffin ('96, '99) on *Thalassema*. Erlanger ('97, 5) endeavours to show that in the mitosis of embryonic cells in the cephalopods (*Sepia*), where the inpushing of the membrane was previously shown by Watasé, the entire spindle arises from the nucleus.

spond in function to those of the central spindle and to the mantle-fibres. It seems probable that the difference between the two types of spindle-formation may be due to, or is correlated with, the fact that the nuclear transformation takes place relatively earlier in the first type. When the nucleus lags behind the spindle-formation the centrosomes take up their position prematurely, as it were, the central spindle disappearing to make way for the nucleus.

It is in the mitosis of plant-cells that the most remarkable type of achromatic figure has been observed. In some of the lower forms (Algæ) mitosis has been clearly shown to conform nearly to the process observed in animal cells, the amphiaster being provided with very large asters and distinct centrosomes, and its genesis corresponding broadly with the second type described above (Figs. 32, 33), though with some interesting modifications of detail.[1] Swingle ('97) describes in *Stytopocaulon* a process closely similar to that seen in many animal cells, the minute but very distinct centrosomes being surrounded by quite typical cytoplasmic asters, passing to opposite poles of the nucleus, and a spindle then developing between them out of the achromatic nuclear substance (Fig. 32). In the flowering plants and pteridophytes, on the other hand, mitosis seems to be of a quite different type, apparently taking place *in the entire absence of centrosomes*. Guignard ('91, 1, '92, 2) clearly described and figured typical centrosomes and attraction-spheres both in the ordinary mitosis (Fig. 34) and in the fertilization of the higher plants, giving an account of their behaviour nearly agreeing with the views then prevailing among zoölogists. Although these accounts have been supported by some other workers,[2] and have recently been in part reiterated by Guignard himself ('98, 1), they have not been sustained by some of the best and most careful later observers, who describe a mode of spindle-formation differing radically from that seen in thallophytes and in animals generally.[3] According to these observations, begun by Farmer and Belajeff, and strongly sustained by the careful studies of Osterhout, Mottier, Nemec, and others, the achromatic figure is almost wholly of cytoplasmic origin, arising from a fibrillar material ("kinoplasm" or "filar plasm," of Strasburger), which at the beginning of mitosis forms a net-like mass surrounding the nucleus, from which fibrillæ radiate out into the cytoplasm. As the nuclear membrane fades, these fibrillæ, continually increasing, invade the nuclear area, gather themselves into bundles, converging to a number of centres (without centrosomes), and thus give rise to an irregular multipolar figure (Figs. 36, 133). This figure finally resolves itself into a definite bipolar spindle which is devoid of centrosomes, and in the earlier stages also of asters, though in the later phases somewhat irregular asters are formed. On the basis of these observations Mottier[1] proposes to distinguish provisionally two well-defined types of mitosis in plants which he designates as the "thallophyte" and the "cormophyte" types. The latter seems wholly irreconcilable with the process observed in animal-cells; for the whole course of spindle-formation seems diametrically opposed in the two cases, and should the cormophyte-type be established it would, to say the least, greatly restrict the application of the centrosome-theory of Van Beneden and Boveri. Only future research can definitely determine the question. There can be no doubt that the descriptions of Guignard and his followers do not rest upon pure imagination; for it is easy to observe at the spindle-poles in some preparations (*e.g.* sections of root-tips of *Allium*, *Lilium*, etc.) deeply staining-bodies such as these authors describe. These "centrosomes" seem, however, to be of quite inconstant occurrence; and the careful studies of Osterhout, Mottier, and Nemec seem to give good ground for the conclusion that they have no such significance as the centrosomes of lower plants or of animals. It should nevertheless be borne in mind that true centrosomes ("blepharoplasts") have been demonstrated in the spermatogenic divisions of some of the vascular cryptogams, and that analogous bodies occur in the corresponding divisions of the cycads (p. 175). We should therefore still hold open the possibility that centrosomes may occur in the vegetative mitoses of the higher plants, their apparent absence being possibly due to lack of staining-capacity or similar conditions rendering their demonstration difficult.[2]

---

[1] See especially Swingle ('97) on *Sphacelariaceæ*, Strasburger ('97) on *Fucus*, Mottier ('98) on *Dictyota; cf.* also Harper ('97) on *Erysiphe* and *Peziza*.

[2] *Cf.* Schaffner ('98), Fulmer ('98).

[3] See Osterhout ('97) on *Equisetum*, Mottier ('97, 1, '97, 2) on *Lilium*, Lawson ('98) on *Cobæa*, Nemec ('99) on *Allium*, Debski ('97, '99) on *Chara;* also Belajeff ('94) and Farmer ('95).

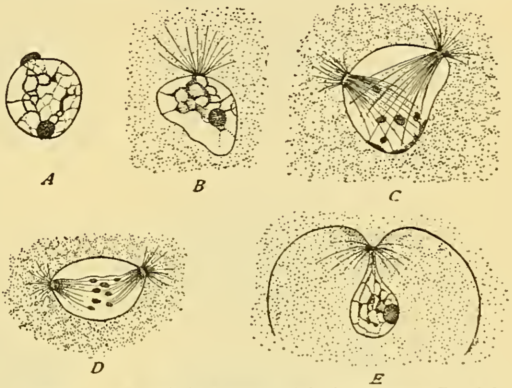

Fig. 33. — Mitosis in ascus-nuclei of a fungus, *Erysiphe*. [HARPER.]

A. Resting nucleus with disc-shaped centrosome (*c*). *B.* Early prophase with aster. *C.* Later prophase; amphiaster; intranuclear spindle forming. *D.* Spindle established. *E.* Daughter-nucleus after division; spore-membrane developing from astral rays.

---

[1] '97, 2, p. 183.

[2] Mention may here be made of the barrel-shaped truncated spindles described in some of the plants. In *Basidiobolus*, Fairchild ('97) finds spindles of this type, having no asters

A no less remarkable mode of spindle-formation, which is in a certain way intermediate between the cormophyte-type and the usual animal type is described by Mead ('97, '98, 1) in the first maturation-division of *Chætopterus*. Here the completed amphiaster is of quite typical form, and the centrosomes persist for the following mitosis; yet Mead is convinced that the amphiaster is synthetically formed by the union of two separate asters and centrosomes (Fig. 150) which have no genetic connection, arising independently *de novo* in the cytoplasm.[1] Improbable as such a conclusion may seem on *a priori* grounds, it is supported by very strong evidence,[2] and, taken together

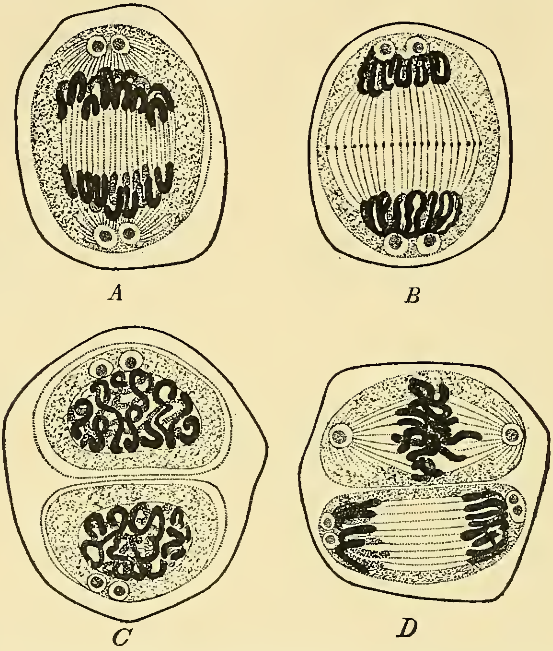

Fig. 34. — Division of pollen-mother-cells in the lily as described by GUIGNARD.

A. Anaphase of the first division, showing the twelve daughter-chromosomes on each side, the interzonal fibres stretching between them, and the centrosomes, already double, at the spindle-poles. *B.* Later stage, showing the cell-plate at the equator of the spindle and the daughter-spiremes (dispireme-stage of Flemming). *C.* Division completed; double centrosomes in the resting cell. *D.* Ensuing division in progress; the upper cell at the close of the prophases, the chromosomes and centrosomes still undivided; lower cell in the late anaphase, cell-plate not yet formed.

---

and nearly parallel fibres, each of which terminates in a deeply staining granule. Nearly similar spindles have been described by Strasburger ('80) in *Spirogyra*, and in the embryo-sac of *Monotropa*. It is not impossible that such spindles may represent a type intermediate between the "cormoptyte" and "thallophyte" types of Mottier.

[1] *Cf.* p. 306.

[2] I have had the privilege of examining some of Mead's beautiful preparations.

with the facts described in plants, it indicates that the forces involved in spindle-formation are far more complex than Van Beneden's and Boveri's hypothesis would lead one to suppose.[1]

The centrosome and centrosphere appear to present great variations that have not yet been thoroughly cleared up and will be more critically discussed beyond.[2] They are known to undergo extensive changes in the cycle of cell-division and to vary greatly in different forms (Fig. 152). In some cases the aster contains at its centre nothing more than a minute deeply staining granule, which doubtless represents the centrosome alone. In other cases the granule is surrounded by a larger body, which in turn lies within the centrosphere or attraction-sphere. In still other cases the centre of the aster is occupied by a large reticular mass, within which no smaller body can be distinguished (*e.g.* in pigment-cells); this mass is sometimes called the centrosome, sometimes the centrosphere. Sometimes, again, the spindle-fibres are not focussed at a single point, and the spindle

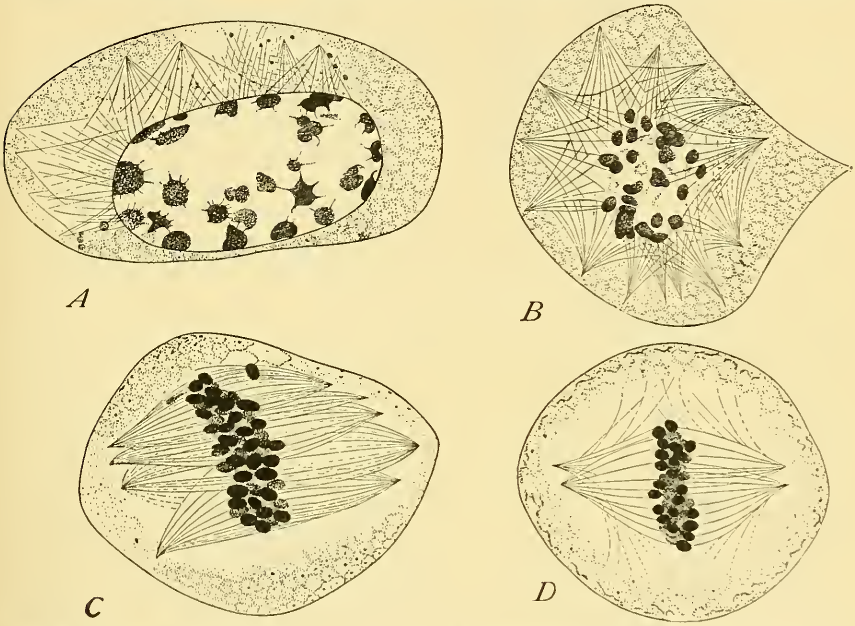

Fig. 36. — Division of spore-mother-cells in *Equisetum*, showing spindle-formation. [OSTERHOUT.]
A. Early prophase, "kinoplasmic" fibrillæ in the cytoplasm. *B*. Multipolar fibrillar figure invading the nuclear area, after disappearance of the nuclear membrane. *C*. Multipolar spindle. *D*. Quadripolar spindle which finally condenses into a bipolar one.

---

[1] See p. 276 for the peculiar spindles, devoid of asters, observed during the maturation of the egg in certain forms. *Cf.* also Morgan's experiments on the artificial production of asters and centrosomes, p. 307.

[2] See p. 304.

appears truncated at the ends, its fibres terminating in a transverse row of granules (maturation-spindles of *Ascaris*, and some plant-cells). It is not entirely certain, however, that such spindles observed in preparations represent the normal structure during life.

b. The Chromatic Figure. — The variations of the chromatic figure must for the most part be considered in the more special parts of this work. There seems to be no doubt that a single continuous spireme-thread may be formed (*cf.* p. 113), but it is equally certain that the thread may appear from the beginning in a number of distinct segments, *i.e.* as a segmented spireme, and there are some cases in which no distinct spireme can be seen, the reticulum resolving itself directly into the chromosomes. The chromosomes, when fully formed, vary greatly in appearance. In many of the tissues of adult plants and animals they are rod-shaped and are often bent in the middle like a V (Figs. 28, 131). They often have this form, too, in embryonic cells, as in the segmentation-stages of the egg in *Ascaris* (Fig. 31) and other forms. The rods may, however, be short and straight (segmenting eggs of echinoderms, etc.), and may be reduced to spheres, as in the maturation-stages of the germ-cells. In the equatorial plate the V-shaped chromosomes are placed with the apex of the V turned toward the spindle (Fig. 28), while the straight rods are placed with one end toward the spindle. In either case the daughter-chromosomes first begin to move apart at the point nearest the spindle, the separation proceeding thence toward the free portion. The V-shaped chromosomes, opening apart from the apex, thus give rise in the early anaphase to <>-shaped figures; while rod-shaped chromosomes often produce λ- and ⊥-shaped figures (the stem of the ⊥ being double). The latter, opening farther apart, form straight rods twice the length of the original chromosome (since each consists of two daughter-chromosomes joined at one end). This rod finally breaks across the middle, thus giving the deceptive appearance of a transverse instead of a longitudinal division (Fig. 52). The <>-shaped figures referred to above are nearly related to those that occur in the so-called *heterotypical mitosis*. Under this name Flemming ('87) first described a peculiar modification of the division of the chromosomes that has since been shown to be of very great importance in the early history of the germ-cells, though it is not confined to them. In this form the chromosomes split at an early period, but the halves remain united by their ends. Each double chromosome then opens out to form a closed ring (Fig. 37), which by its mode of origin is shown to represent two daughter-chromosomes, each forming half of the ring, united by their ends. The ring finally breaks in two to form two U-shaped chromosomes which diverge to opposite poles of the spindle as usual. As will be shown in Chapter V., the divisions by which the germ-cells are matured are in many cases of this type; but the primary rings here in many cases represent not two but four chromosomes, into which they afterward break up.

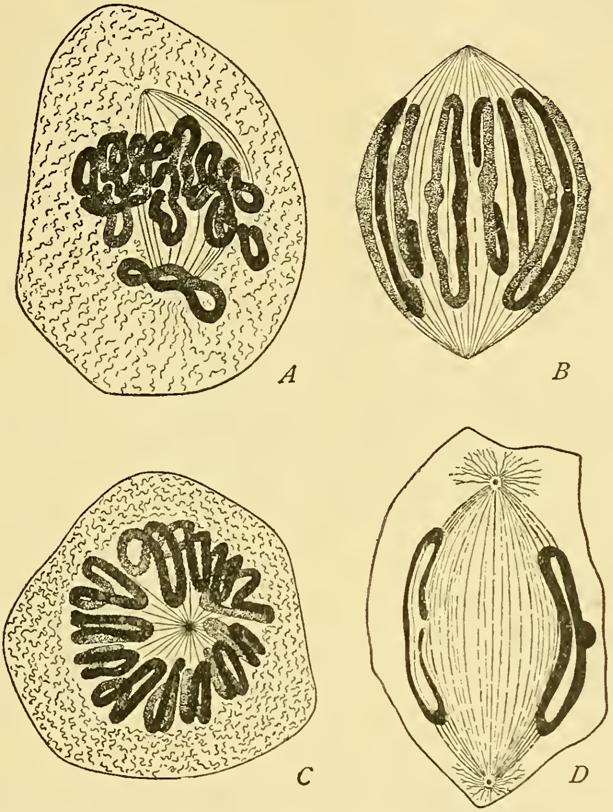

Fig. 37. — Heterotypical mitosis in spermatocytes of the salamander. [FLEMMING.]

A. Prophase, chromosomes in the form of scattered rings, each of which represents two daughter-chromosomes joined end to end. *B.* The rings ranged about the equator of the spindle and dividing; the swellings indicate the ends of the chromosomes. *C.* The same viewed from the spindle-pole. *D.* Diagram (Hermann) showing the central spindle, asters, and centrosomes, and the contractile mantle-fibres attached to the rings (one of the latter dividing).

2. *Bivalent and Plurivalent Chromosomes*

The last paragraph leads to the consideration of certain variations in the number of the chromosomes. Boveri discovered that the species *Ascaris megalocephala* comprises two varieties which differ in no visible respect save in the number of chromosomes, the germ-nuclei of one form (" variety bivalens " of Hertwig) having two chromosomes, while in the other form ("variety univalens") there is but one. Brauer discovered a similar fact in the phyllopod *Artemia*, the number of somatic chromosomes being 168 in some individuals, in others only 84 (p. 281).

It will appear hereafter that in some cases the primordial germ-cells show only half the usual number of chromosomes, and in *Cyclops* the same is true, according to Häcker, of all the cells of the early cleavage-stages.

In all cases where the number of chromosomes is apparently reduced ("pseudo-reduction" of Rückert) it is highly probable that each chromatin-rod represents not one but two or more chromosomes united together, and Häcker has accordingly proposed the terms *bivalent* and *plurivalent* for such chromatin-rods.[1] The truth of this view, which originated with Vom Rath, is, I think, conclusively shown by the case of *Artemia* described at page 281, and by many facts in the maturation of the germ-cells hereafter considered. In *Ascaris* we may regard the chromosomes of Hertwig's "variety univalens" as really bivalent or double, *i.e.* equivalent to two such chromosomes as appear in "variety bivalens." These latter, however, are probably in their turn plurivalent, *i.e.* represent a number of units of a lower order united together; for, as described at page 148, each of these normally breaks up in the somatic cells into a large number of shorter chromosomes closely similar to those of the related species *Ascaris lumbricoides*, where the normal number is 24.

Häcker has called attention to the striking fact that plurivalent mitosis is very often of the heterotypical form, as is very common in the maturation-mitoses of many animals (Chapter V.), and often occurs in the early cleavages of *Ascaris*; but it is doubtful whether this is a universal rule.

3. *Mitosis in the Unicellular Plants and Animals*

The process of mitosis in the one-celled plants and animals has a peculiar interest, for it is here that we must look for indications of its historical origin. But although traces of mitotic division were seen in the Infusoria by Balbiani ('58–'61), Stein ('59), and others long before it was known in the higher forms, it has only recently received adequate attention and is still imperfectly understood.

Mitotic division has now been observed in many of the main divisions of Protozoa and unicellular plants; but in the present state of the subject it must be left an open question whether it occurs in all. In some of the gregarines and Heliozoa, the process is of nearly or quite the same type as in the Metazoa. From such mitoses, however, various gradations may be traced toward a much simpler process, such as occurs in *Amœba* and the lower flagellates; and it is not improbable that we have here representatives of more primitive conditions. Among the more interesting of these modifications may be mentioned: —

---

[1] The words *bivalent* and *univalent* have been used in precisely the opposite sense by Hertwig in the case of *Ascaris*, the former term being applied to that variety having *two* chromosomes in the germ-cells, the latter to the variety with one. These terms certainly have priority, but were applied only to a specific case. Häcker's use of the words, which is strictly in accordance with their etymology, is too valuable for general descriptive purposes to be rejected.

1. Even in forms that nearly approach the mitosis of higher types the nuclear membrane may persist more or less completely through every stage (*Noctiluca*, *Euglypha*, *Actinosphærium*).

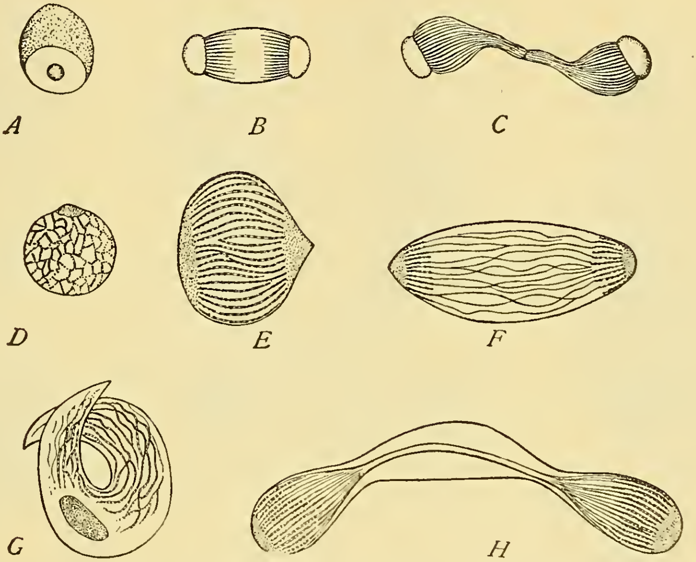

Fig. 38. — Mitotic division in Infusoria. [R. HERTWIG.]

A–C. Macronucleus of *Spirochona*, showing pole-plates. *D–H.* Successive stages in the division of the micronucleus of *Paramæcium*. *D.* The earliest stage, showing reticulum. *G.* Following stage ("sickle-form") with nucleolus. *E.* Chromosomes and pole-plates. *F.* Late anaphase. *H.* Final phase.

2. Asters may be present (Heliozoa, gregarines) or wanting (Infusoria, Radiolaria).

3. In one series of forms the centrosome or sphere is represented by a persistent intranuclear body (nucleolo-centrosome) of considerable size, which divides to form a kind of central spindle (*Euglena Amœba*, Infusoria?).

4. In a second series the centrosome or sphere is a persistent

extranuclear body, as in most Metazoa (*Heliozoa, Noctiluca, Paramœba*).

5. In a few forms having a scattered nucleus the chromatin-granules are only collected about the apparently persistent sphere or centrosome at the time of its division, and afterward scatter through the cell, leaving the sphere lying in the general cell-substance (*Tetramitus*).

6. The arrangement of the chromatin-granules to form chromosomes appears to be of a secondary importance as compared with higher forms, and the essential feature in nuclear division appears to be the fission of the individual granules.

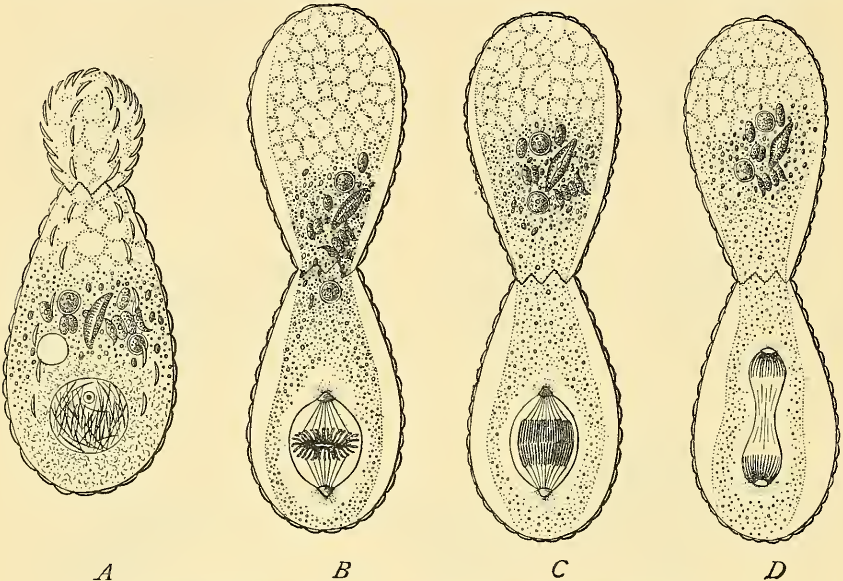

Fig. 39. — Mitosis in the rhizopod, *Euglypha*. [SCHEWIAKOFF.]

In this form the body is surrounded by a firm shell which prevents direct constriction of the cell-body. The latter therefore divides by a process of budding from the opening of the shell (the initial phase shown at *A*); the nucleus meanwhile divides, and one of the daughter-nuclei afterward wanders out into the bud.

A. Early prophase; nucleus near lower end containing a nucleolus and numerous chromosomes. *B*. Equatorial plate and spindle formed inside the nucleus; pole-bodies or pole-plates (*i.e.* attraction-spheres or centrosomes) at the spindle-poles. *C*. Metaphase. *D*. Late anaphase, spindle dividing; after division of the spindle the outer nucleus wanders out into the bud.

We may first consider especially the achromatic figure. The basis of our knowledge in this field was laid by Richard Hertwig through his studies on an infusorian, *Spirochona* ('77), and a rhizopod, *Actinosphærium* ('84). In both these forms a typical spindle and equatorial plate are formed *inside the nuclear membrane* by a direct transformation of the nuclear substance. In *Spirochona* (Fig. 38, *A–C*) a hemispherical "end-plate" or "pole-plate" is situated at either pole of the spindle, and Hertwig's observations indicated, though they did not prove, that these plates arose by the division of a large "nucleolus." Nearly similar pole-plates were somewhat described by Schewiakoff ('88) in *Euglypha* (Fig. 39), and it seems clear that they are the analogues of the centrosomes or attraction-spheres in higher forms. In *Euglena*, as shown by Keuten, the pole-plates, or their analogues, certainly arise by division of a distinct and persistent intranuclear body ("nucleolus" or "nucleolo-centrosome") which elongates to form a kind of central spindle around which the chromatin elements are grouped (Fig. 40); and Schaudinn ('95) described a similar process in *Amœba*. Richard Hertwig's latest work on *Infusoria* ('95) indicates that a similar process occurs in the micronuclei of *Paramœcium*, which at first contain a large "nucleolus" and afterward a conspicuous pole-plate at either end of the spindle (Fig. 38, *D–H*). The origin of the pole-plates was not, however, positively determined. A corresponding dividing body is found in *Ceratium* (Lauterborn, '95), and as in the Infusoria the entire nucleus transforms itself into a fibrillar spindle-like body.

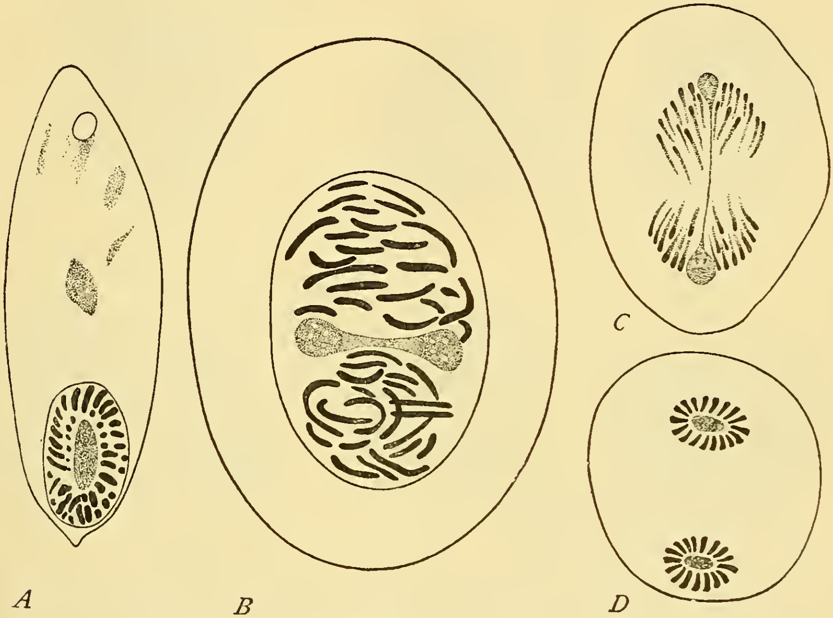

Fig. 40.— Mitosis in the flagellate, *Euglena*. [KEUTEN.]

A. Preparing for division; the nucleus contains a "nucleolus" or nucleolo-centrosome surrounded by a group of chromosomes. *B*. Division of the "nucleolus" to form an intranuclear spindle. *C*. Later stage. *D*. The nuclear division completed.

Still simpler conditions are found in some of the flagellates.[1] In *Chilomonas* the sphere may still be regarded as intranuclear, since it lies in the middle of an irregular mass of chromatin-granules, though the latter are apparently not enclosed by a membrane. Nuclear division is here accomplished by fission of the sphere and the aggregation of the chromatin-granules around the two products. In *Tetramitus*, finally (Fig. 16), the nucleus is represented by chromatin-granules that are scattered irregularly through the cell and only at the time of division collect about the dividing sphere.

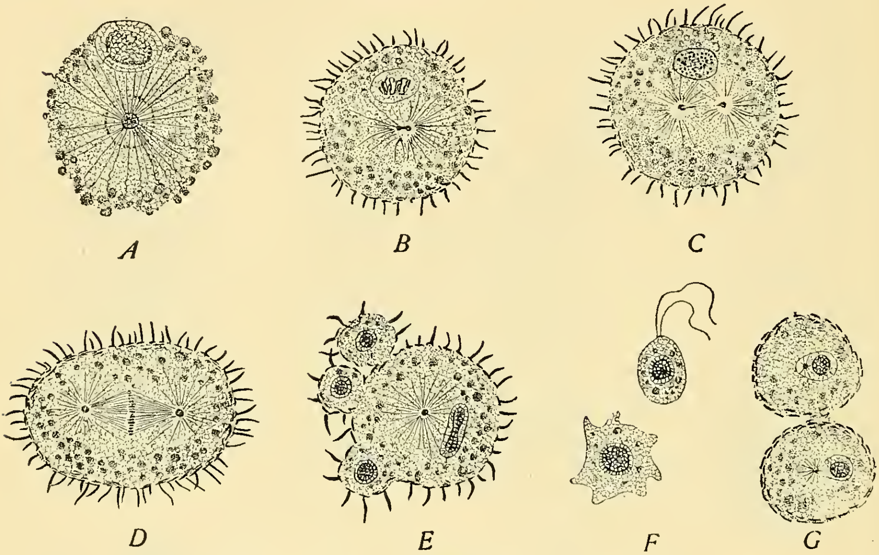

Fig. 41. — Mitosis in the Heliozoa. [SCHAUDINN.]

A. Sphærastrum; vegetative cell showing nucleus, "central granule" (centrosome), and axial rays. *B–G. Acanthocystis.* *B–D.* Prophases of mitosis. *E.* Budding to form swarm-spores. *F.* Swarm-spores, devoid of centrosomes. *G.* Swarm-spores preparing for division; intranuclear origin of centrosome.

In a second series of forms, represented by *Noctiluca* (Ishikawa, '94, '98), (Calkins, '98, 2), *Paramœba* (Schaudinn, '96, 1), *Actinophrys* and *Acanthocystis* (Schaudinn, '96, 2), and the diatoms (Lauterborn, '96), the sphere lies outside the nucleus in the cytoplasm and the mitosis is closely similar to that observed in most Metazoa. This is most striking in the Heliozoa, where the centrosome persists through the vegetative condition of the cell as the "central granule," to which the axial filaments of the pseudopodia converge. Schaudinn ('96, 2) shows that by the division of this body a typical extranuclear amphiaster and central spindle are formed (Fig. 41), while the chromatin passes through a spireme-stage, breaks into very short rod-shaped chromosomes which split lengthwise and arrange themselves in the equator of the spindle, while the nuclear membrane fades away. *Noctiluca* (Fig. 42), as shown by Ishikawa and Calkins, agrees with this in the main points; but the nuclear membrane does not at any period wholly disappear, and a distinct centrosome is found at the centre of the sphere. The latter body, which is very large, gives rise by a division to a fibrillated central spindle, about which the nucleus wraps itself while mantle-fibres are developed from the sphere-substance and become attached to the chromosomes, the nuclear membrane fading away along the surface of contact with the central spindle (Calkins). Broadly speaking, the facts are similar in

---

[1] Calkins, '98, 1, '98, 2.

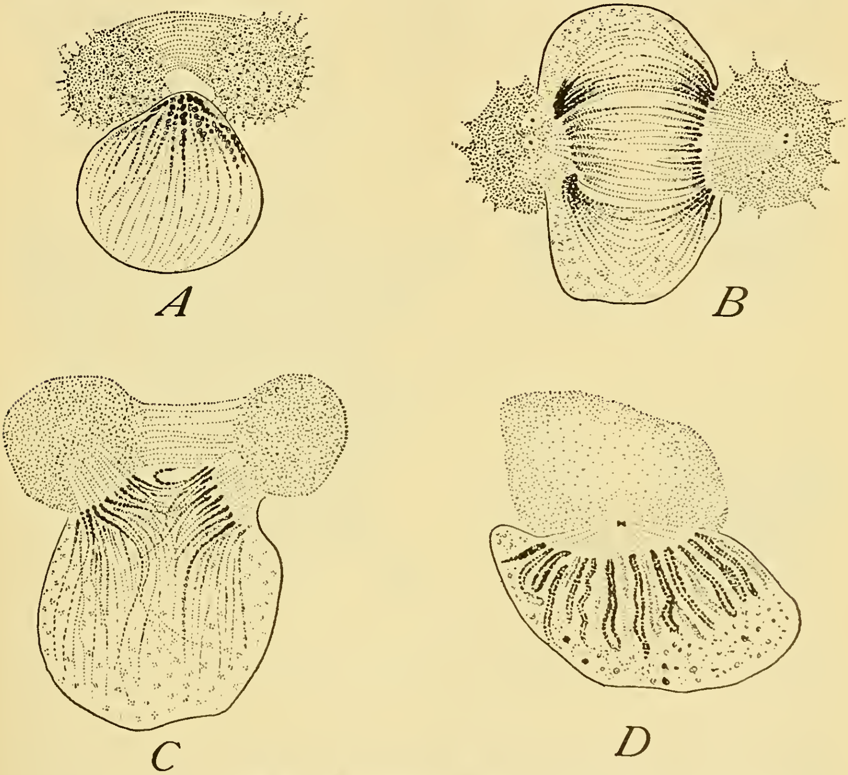

Fig. 42. — Mitosis in *Noctiluca*. [CALKINS.]

A. Prophase; division of the sphere to form the central spindle; chromosomes converging to the nuclear pole. *B*. Late anaphase, in horizontal section, showing centrosomes; the central spindle has sunk into the nucleus; nuclear membrane still intact except at the poles. *C*. Early anaphase; mantle-fibres connected with the diverging chromosomes. *D*. Final anaphase (which is also the initial prophase of the succeeding division of spore-forming mitosis); doubling of centrosome and splitting of chromosomes.

the diatoms (*Surirella*, *t.* Lauterborn), where the central spindle, arising by a peculiar process from an extranuclear centrosome, (sphere ?) sinks into the nucleus in a manner strongly suggesting that observed in *Noctiluca*.

In the interesting form *Paramœba*, as described by Schaudinn ('96, 1), the sphere ("Nebenkörper"), which is nearly as large as the nucleus, divides to form a central spindle, about the equator of which the chromatin-elements become arranged in a ring (Fig. 43); but no centrosome has yet been demonstrated in the sphere. *Paramœba* appears to differ from *Euglena* mainly in the fact that at the close of division the sphere is in the former left outside the daughter-nucleus and in the latter enclosed within it.[1] The connecting link is perfectly given by *Tetramitus*, where no morphological nucleus is formed, and the sphere lies in the general cell-substance (p. 92); and we could have no clearer demonstration that the extra- or intranuclear position of sphere or centrosome is of quite secondary importance. As regards the formation of the spheres (pole-plates) *Actinosphærium* (Figs. 44, 45) seems to show a simpler condition than any of the above forms, since no permanent sphere exists, and Brauer ('94) and R. Hertwig ('98) agree that the pole-plates are formed by a gradual accumulation of the achromatic substance of the nucleus at opposite poles.

A distinct centrosome (centriole ?) in the interior of the sphere has thus far only been observed in a few forms (*Noctiluca*, *Actinosphærium*), and neither its origin nor its relation to the sphere has yet been sufficiently cleared up. Both Ishikawa ('94) and Calkins ('98, 2) somewhat doubtfully concluded that in *Noctiluca* the centrosomes arise within the nucleus, migrating thence out into the extranuclear sphere. With this agree R. Hertwig's latest studies on *Actinosphærium* ('98), the spindle-poles being first formed from the pole-plates (themselves of nuclear origin), and the centrosomes then passing into them from the nucleus. Hertwig reaches the further remarkable conclusion that the centrosomes arise as portions of the *chromatin-network* extruded at the nuclear poles (Fig. 45), first forming a spongy irregular mass, but afterward condensing into a deeply staining pair of granules which pass to the respective poles of the spindle. It is a remarkable fact that these centrosomes are only found in the two maturation-divisions, and are absent from the ordinary vegetative mitoses where the spindle-poles are formed by two cytoplasmic masses derived, as Hertwig believes, from the intranuclear plates. Schaudinn ('96, 3) likewise describes and clearly figures an intranuclear origin of the centrosome in buds of *Acanthocystis* (Fig. 41), which are derived by direct division of the mother-nucleus with no trace of a centrosome. In this same form, as described above, the ordinary vegetative mitoses are quite of the metazoan type, with a persistent extranuclear centrosome.

---

[1] *Cf.* Calkins, '98, 1, p. 388.

The history of the chromatin in the mitosis of unicellular forms shows some interesting modifications. In a considerable number of forms a more or less clearly marked spireme-stage precedes the formation of chromosomes (diatoms, Infusoria, dinoflagellates, *Euglypha*); in others, long chromosomes are formed without a distinct spireme-stage (*Noctiluca*). It has been clearly demonstrated that in some cases these chromosomes split lengthwise, as in Metazoa (*Noctiluca*, diatoms, *Actinophrys*, probably in *Euglypha*); but in some cases they are stated to divide transversely in the middle (Infusoria according to Hertwig, *Ceratium* according to Lauterborn). These chromosomes appear always to arise, as in Metazoa, through the linear arrangement of chromatin-granules (*Noctiluca*, *Actinosphærium*, *Euglena*), which themselves in many cases arise by the preliminary fragmentation of one or more large chromatin-masses (*e.g.* in *Noctiluca* or *Actinosphærium*). In other forms no such linear aggregates are formed, and direct fission of the chromatin-granules appears to take place without the formation of bodies morphologically comparable with the chromosomes of such forms as *Noctiluca*. This is apparently the case in *Tetramitus*, and *Achromatium*, other forms having a distributed

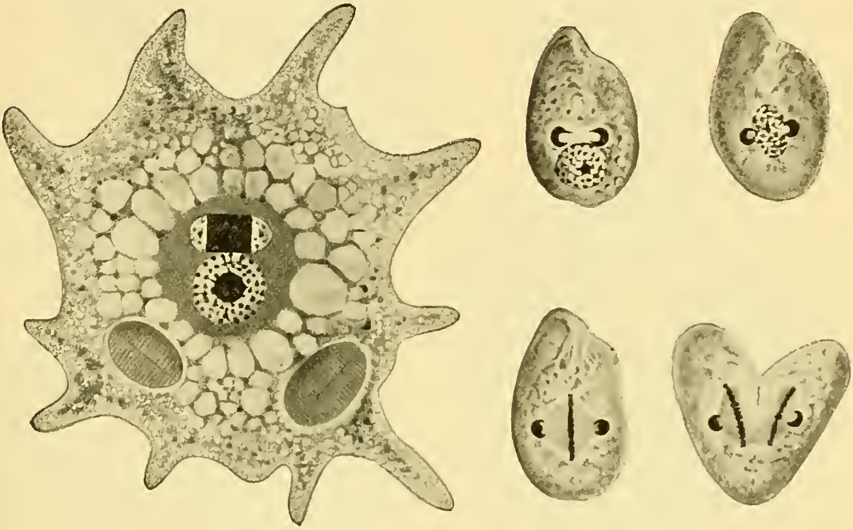

Fig. 43. — Mitosis in *Paramœba*. [SCHAUDINN.]

At the left, amœboid phase, showing nucleus and "Nebenkörper." At the right, four stages of division in the swarm-spores.

nucleus,[1] and in such forms as *Chilomonas* and *Trachelomonas*, where the granules are permanently aggregated about a central body. Too little is known of the facts to justify a very positive statement; but on the whole they point toward the conclusion that in the simplest types of mitosis no true chromosome-formation occurs, thus sustaining Brauer's conclusion that the essential fact in the history of the chromatin in mitosis is the fission of the individual granules.[2]

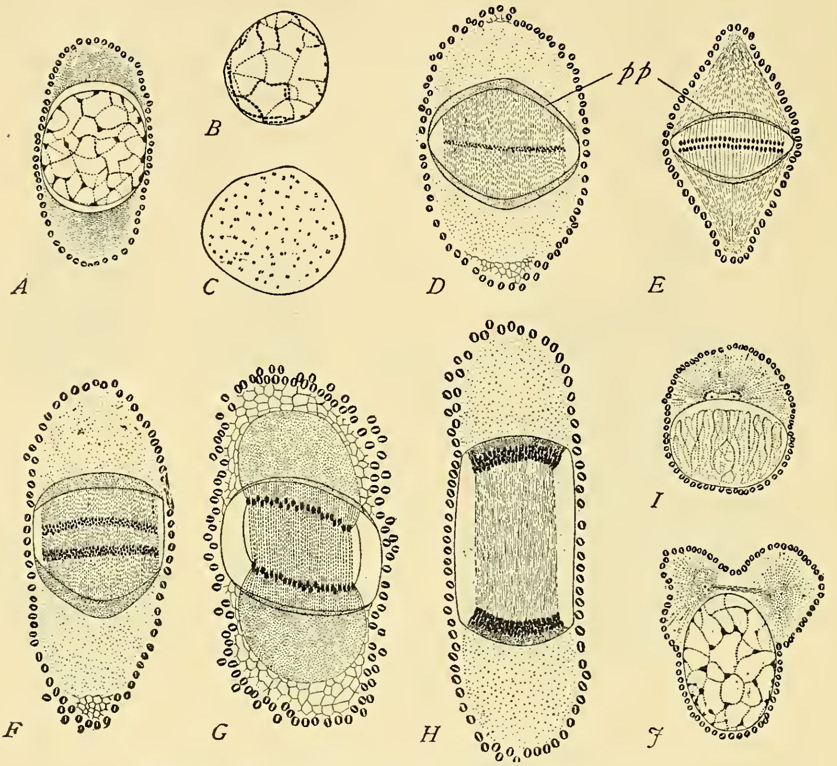

Fig. 44. — Mitosis in the rhizoped *Actinosphærium*. [BRAUER.]

A. Nucleus and surrounding structures in the early prophase; above and below the reticular nucleus lie the semilunar "pole-plates," and outside these the cytoplasmic masses in which the asters afterward develop. *B*. Later stage of the nucleus. *D*. Mitotic figure in the metaphase, showing equatorial plate, intra-nuclear spindle, and pole-plates (*p.p.*). *C*. Equatorial plate, viewed *en face*, consisting of double chromatin-granules. *E*. Early anaphase. *F. G*. Later anaphases. *H*. Final anaphase. *I*. Telophase; daughter-nucleus forming, chromatin in loop-shaped threads; outside the nuclear membrane the centrosome, already divided, and the aster. *J*. Later stage; the daughter-nucleus established; divergence of the centrosomes. Beyond this point the centrosomes have not been followed.

---

[1] The fission of the individual granules is carefully described and figured by Schewiakoff in *Achromatium*.

[2] For speculations on the historical origin of the centrosome, etc., see p. 315.

4. *Pathological Mitoses*

Under certain circumstances the delicate mechanism of cell-division may become deranged, and so give rise to various forms of pathological mitoses. Such a miscarriage may be artificially produced, as Hertwig, Galeotti, and others have shown, by treating the dividing cells with poisons and other chemical substances (quinine, chloral, nicotine, potassic iodide, etc.). Pathological mitoses may, however, occur without discoverable external cause; and it is a very interesting fact, as Klebs, Hansemann, and Galeotti have especially pointed out, that they are of frequent occurrence in abnormal growths such as cancers and tumours.

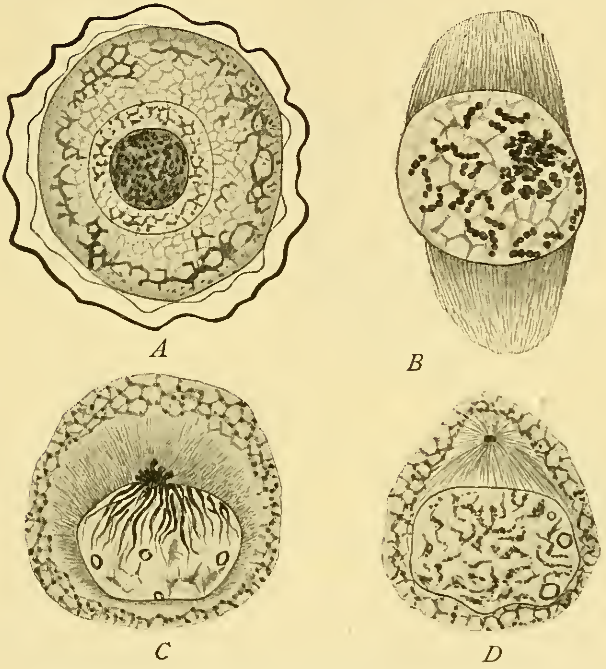

Fig. 45. — Mitosis in *Actinosphærium*. [R. HERTWIG.]

A. Encysted form, with resting nucleus; chromatin aggregated into large nucleolus-like body. *B*. prophase of division of the encysted form, showing chromosome-like bodies formed of granules, and spindle without centrosomes. *C*. Earlier prophase of the first maturation division, showing extrusion of chromatic substance to form the centrosome. *D*. Later stage, showing centrosome and aster.

The abnormal forms of mitoses are arranged by Hansemann in two general groups, as follows: (1) *asymmetrical mitoses*, in which the chromosomes are unequally distributed to the daughter-cells, and (2) *multipolar mitoses*, in which the number of centrosomes is more than two, and more than one spindle is formed. Under the first group are included not only the cases of unequal distribution of the daughter-chromosomes, but also those in which chromosomes fail to be drawn into the equatorial plate and hence are lost in the cytoplasm.

Klebs first pointed out the occurrence of asymmetrical mitoses in carcinoma-cells, where they have been carefully studied by Hansemann and Galeotti. The inequality is here often extremely marked, so that one of the daughter-cells may receive more than twice as much chromatin as the other (Fig. 46). Hansemann, whose conclusions are accepted by Galeotti, believes that this asymmetry of mitosis gives an explanation of the familiar fact that in cancer-cells many of the nuclei are especially rich in chromatin (hyperchromatic cells), while others are abnormally poor (hypochromatic cells). Lustig and Galeotti ('93) showed that the unequal distribution of chromatin is correlated with and probably caused by a corresponding inequality in the centrosomes which causes an asymmetrical development of the amphiaster. A very interesting discovery made by Galeotti ('93) is that asymmetrical mitoses, exactly like those seen in carcinoma, may be artificially produced in the epithelial cells of salamanders (Fig. 47) by treatment with dilute solutions of various drugs (antipyrin, cocaine, quinine).

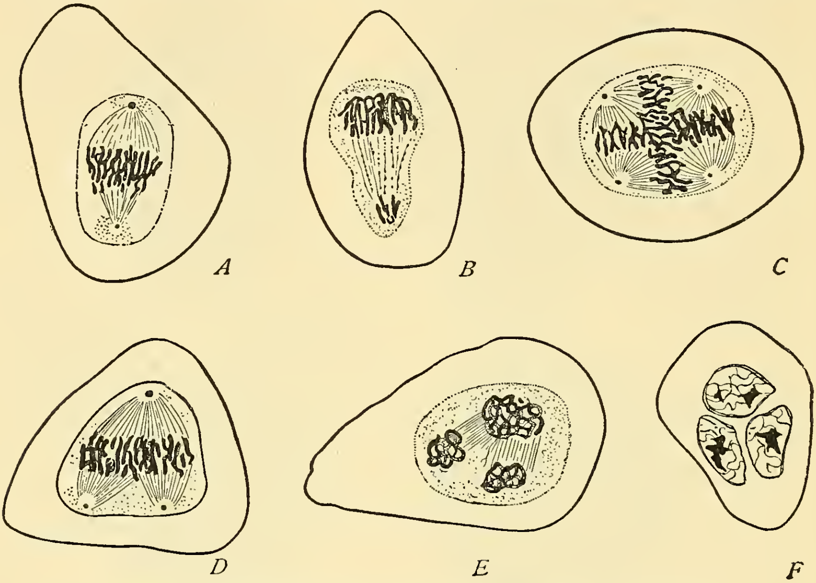

Fig. 46. — Pathological mitoses in human cancer-cells. [GALEOTTI.]

A. Asymmetrical mitosis with unequal centrosomes. *B*. Later stage, showing unequal distribution of the chromosomes. *C*. Quadripolar mitosis. *D*. Tripolar mitosis. *E*. Later stage. *F*. Trinucleate cell resulting.

Normal multipolar mitoses, though rare, sometimes occur, as in the division of the pollen-mother-cells and the endosperm-cells of flowering plants (Strasburger); but such mitotic figures arise through the union of two or more bipolar amphiasters in a syncytium and are due to a rapid succession of the nuclear divisions unaccompanied by fission of the cell-substance. These are not to be confounded with pathological mitoses arising by premature or abnormal division of the centrosome. If one centrosome divide, while the other does not, triasters are produced, from which may arise three cells or a trinucleated cell. If both centrosomes divide, tetrasters or polyasters are formed. Here again the same result has been artificially attained by chemical stimulus (*cf.* Schottländer, '88). Multipolar mitoses are also common in regenerating tissues after irritative stimulus (Ströbe); but it is uncertain whether such mitoses lead to the formation of normal tissue.[1]

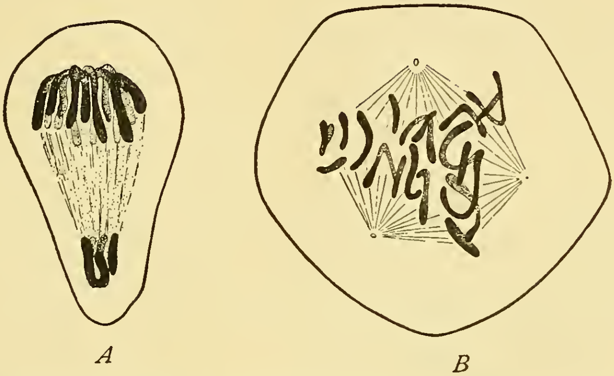

Fig. 47. — Pathological mitoses in epidermal cells of salamander caused by poisons. [Galeotti.]

A. Asymmetrical mitosis after treatment with 0.05% antipyrin solution. *B.* Tripolar mitosis after treatment with 0.5% potassic iodide solution.

The frequency of abnormal mitoses in pathological growths is a most suggestive fact, but it is still wholly undetermined whether the abnormal mode of cell-division is the cause of the disease or the reverse. The latter seems the more probable alternative, since normal mitosis is certainly the rule in abnormal growths; and Galeotti's experiments suggest that the pathological mitoses in such growths may be caused by the presence of deleterious chemical products in the diseased tissue, and perhaps point the way to their medical treatment.

---

[1] The remarkable polyasters formed in polyspermic fertilization of the egg are described at page 198.

D. The Mechanism of Mitosis

We now pass to a consideration of the forces at work in mitotic division, which leads us into one of the most debatable fields of cytological inquiry.

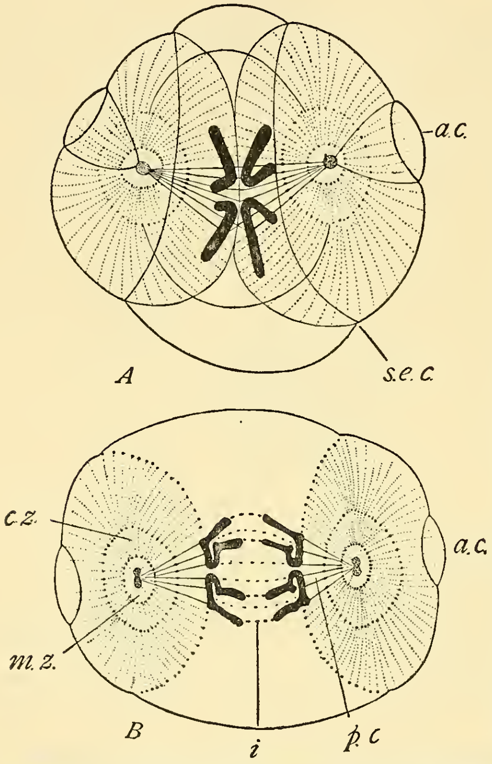

Fig. 48. — Slightly schematic figures of dividing eggs of *Ascaris*, illustrating Van Beneden's theory of mitosis. [Van Beneden and Julin.]

A. Early anaphase; each chromosome has divided into two. *B*. Later anaphase during divergence of the daughter-chromosomes. *a.c.* Antipodal cone of astral rays; *c.z.* cortical zone of the attraction-sphere; *i.* interzonal fibres stretching between the daughter-chromosomes; *m.z.* medullary zone of the attraction-sphere; *p.c.* principal cone, forming one-half of the contractile spindle (the action of these fibres is reënforced by that of the antipodal cone); *s.e.c.* subequatorial circle, to which the astral rays are attached.

1. *Function of the Amphiaster*

All observers agree that the amphiaster is in some manner an expression of the forces by which cell-division is caused, and many accept, in one form or another, the first view clearly stated by Fol,[1] that the asters represent in some manner centres of attractive forces focussed in the centrosome or dynamic centre of the cell. Regarding the nature of these forces, there is, however, so wide a divergence of opinion as to compel the admission that we have thus far accomplished little more than to clear the ground for a precise investigation of the subject; and the mechanism of mitosis still lies before us as one of the most fascinating problems of cytology.

(*a*) *The Theory of Fibrillar Contractility.* — The view that has taken the strongest hold on recent research is the hypothesis of *fibrillar contractility*. First suggested by Klein in 1878, this hypothesis was independently put forward by Van Beneden in 1883, and fully outlined by him four years later in the following words: "In our opinion all the internal movements that accompany cell-division have their immediate cause in the contractility of the protoplasmic fibrillæ and their arrangement in a kind of radial muscular system, composed of antagonizing groups" (*i.e.* the asters with their rays). "In this system the central corpuscle (centrosome) plays the part of an organ of insertion. It is the first of all the various organs of the cells to divide, and its division leads to the grouping of the contractile elements in two systems, each having its own centre. The presence of these two systems brings about cell-division, and actively determines the paths of the secondary chromatic asters" (*i.e.* the daughter-groups of chromosomes) "in opposite directions. An important part of the phenomena of (karyo-) kinesis has its efficient cause, not in the nucleus, but in the protoplasmic body of the cell."[1] This beautiful hypothesis was based on very convincing evidence derived from the study of the *Ascaris* egg, and it was here that Van Beneden first demonstrated the fact, already suspected by Flemming, that the daughter-chromosomes move apart to the poles of the spindle and give rise to the two respective daughter-nuclei.[2]

---

[1] '73, p. 473.

Van Beneden's general hypothesis was accepted in the following year by Boveri ('88, 2), who contributed many important additional facts in its support, though neither his observations nor those of later investigators have sustained Van Beneden's account of the grouping of the astral rays. Boveri showed in the clearest manner that, during the fertilization of *Ascaris*, the astral rays become attached to the chromosomes of the germ-nuclei; that each comes into connection with rays from both the asters; that the chromosomes, at first irregularly scattered in the egg, are drawn into a position of equilibrium in the equator of the spindle by the shortening of these rays (Figs. 90, 147); and that *the rays thicken as they shorten.* He showed that as the chromosome splits, each half is connected only with rays (spindle-fibres) from the aster on its own side; and he followed, step by step, the shortening and thickening of these rays as the daughter-chromosomes diverge. In all these operations the behaviour of the rays is precisely like that of muscle-fibres; and it is difficult to study Boveri's beautiful figures and clear descriptions without sharing his conviction that "of the contractility of the fibrillæ there can be no doubt."[1]

---

[1] '87, p. 280.

[2] '83, p. 544. Van Beneden describes the astral rays, both in *Ascaris* and in tunicates, as differentiated into several groups. One set, forming the "principal cone," are attached to the chromosomes and form one-half of the spindle, and, by the contractions of these fibres, the chromosomes are passively dragged apart. An opposite group, forming the "antipodal cone," extend from the centrosome to the cell-periphery, the base of the cone forming the "polar circle." These rays, opposing the action of the principal cones, not only hold the centrosomes in place, but, by their contractions, drag them apart, and thus cause an actual divergence of the centres. The remaining astral rays are attached to the cell-periphery and are limited by a subequatorial circle (Fig. 48). Later observations indicate, however, that this arrangement of the astral rays is not of general occurrence, and that the rays often do not reach the periphery, but lose themselves in the general reticulum.

Very convincing evidence in the same direction is afforded by pigment-cells and leucocytes or wandering cells, in both of which there is a very large permanent aster (attraction-sphere) even in the resting cell. The structure of the aster in the leucocyte, where it was first discovered by Flemming in 1891, has been studied very carefully by Heidenhain in the salamander. The astral rays here extend throughout nearly the whole cell (Fig. 49), and are believed by Heidenhain to represent the contractile elements by means of which the cell changes its form and creeps about. A similar conclusion was reached by Solger ('91) and Zimmermann ('93, 2) in the case of pigment-cells (chromatophores) in fishes. These cells have, in an extraordinary degree, the power of changing their form and of actively creeping about. Solger and Zimmermann have shown that the pigment-cell contains an enormous aster, whose rays extend in every direction through the pigment-mass, and it is almost impossible to doubt that the aster is a contractile apparatus, like a radial muscular system, by means of which the active changes of form are produced (Fig. 50). This interpretation of the aster receives additional support through Schaudinn's ('96, 3) highly interesting dis-

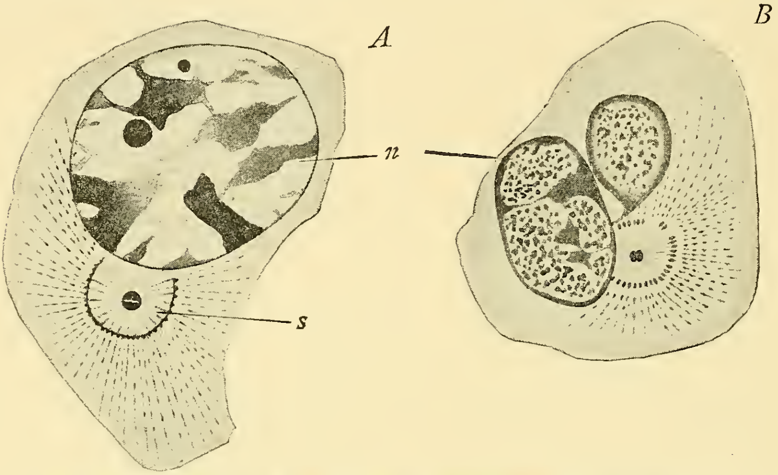

Fig. 49. — Leucocytes or wandering cells of the salamander. [HEIDENHAIN.]

A. Cell with a single nucleus containing a very coarse network of chromatin and two nucleoli (plasmosomes); *s*. permanent aster, its centre occupied by a double centrosome surrounded by an attraction-sphere. *B*. Similar cell, with double nucleus; the smaller dark masses in the latter are oxychromatin-granules (linin), the larger masses are basichromatin (chromatin proper).

---

[1] '88, 2, p. 99.

covery that the "central granule" of the Heliozoa is to be identified with the centrosome and plays the same *rôle* in mitosis (Fig. 41). In these animals the axial filaments of the radiating pseudopodia converge to the central granule during the vegetative state of the cell, thus forming a permanent aster which Schaudinn's observations prove to be directly comparable to that of a leucocyte or of a mitotic figure. There is in this case no doubt of the contractility of the rays, and a strong, if indirect, argument is thus given in favour of contractility in other forms of asters.[1] The contraction-hypothesis is beautifully illustrated by means of a simple and easily constructed model, devised by Heidenhain ('94, '96), which closely simulates some of the phenomena of mitosis. In its simplest form the model consists of a circle, marked on a flat surface, to the periphery of which are attached at equal

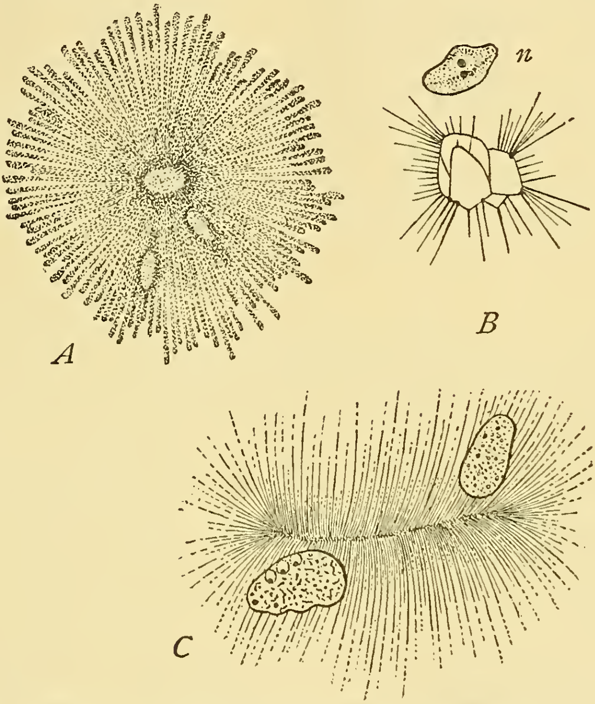

Fig. 50. — Pigment-cells and asters from the epidermis of fishes. [ZIMMERMANN.]

A. Entire pigment-cell, from *Blennius*. The central clear space is the central mass of the aster from which radiate the pigment-granules; two nuclei below. *B*. Nucleus (*n*) and aster after extraction of the pigment, showing reticulated central mass. *C*. Two nuclei and aster with rod-shaped central mass, from *Sargus*.

---

[1] For an interesting discussion and development of the contraction-hypothesis see Watasé, '94.

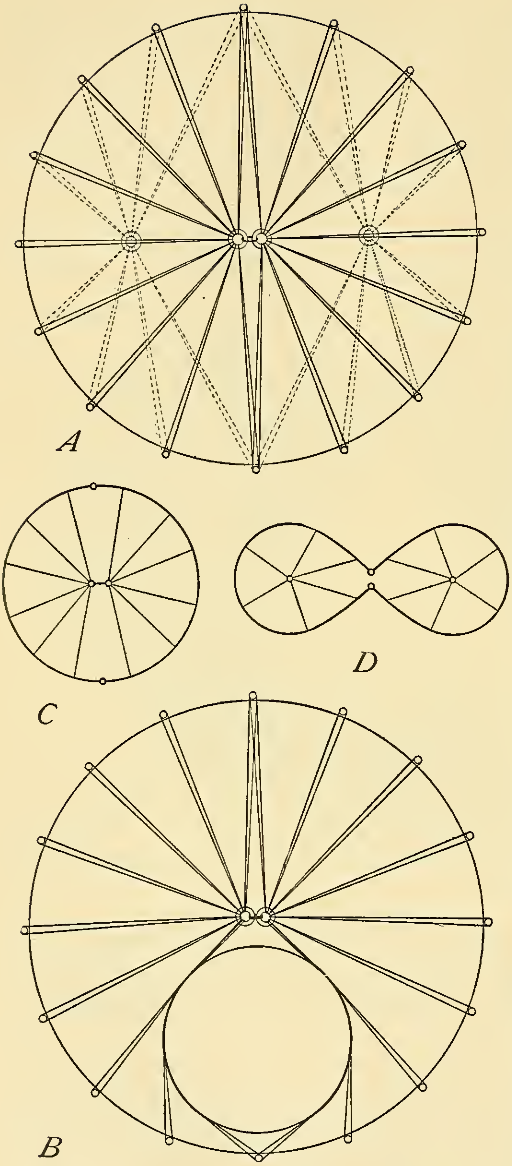

Fig. 51. — Heidenhain's model of mitosis (mainly from HEIDENHAIN).

A. Dotted lines show position of the rays upon severing connection between the small rings. *B.* Position upon insertion of "nucleus." *C. D.* Models with flexible hinged hoops, showing division.

intervals a series of rubber bands (astral rays). At the other ends these bands are attached to a pair of small rings (centrosomes) fastened together. In the position of equilibrium, when the rays are stretched at equal tension, the rays form a symmetrical aster with the centrosomes at the centre of the circle (Fig. 51, *A*). If the connection between the centrosomes be severed, they are immediately dragged apart to a new position of equilibrium with the rays grouped in two asters, as in the actual cell (dotted lines in Fig. 51, *A*). If a round pasteboard box of suitable size (nucleus) be inserted between two of the rays, it assumes an eccentric position, the cell-axis being formed by a line passing through its centre and that of the pair of small rings (*cf.* the epithelial cell, p. 57), and upon division of the aster it takes up a position between the two asters. In a second form of the models the circle is formed of two half rings of flexible steel, joined by hinges; the divergence of the small rings is here accompanied by an elongation and partial constriction of the model in the equatorial plane; and if, finally, the hinge-connection be removed, each half of the ring closes to form a complete ring.[1]

Heidenhain has fully worked out a theory of mitosis based upon the analogy of these pretty models. The astral rays of the cell ("organic radii") are assumed to be in like manner of equal length and in a state of equal tonic contraction or tension, the centrosome forming the common insertion-point of the rays, and equilibrium of the system being maintained by turgor of the cell. Upon disappearance of the nuclear membrane and division of this insertion-point, the tension of the rays causes divergence of the centrosomes and formation of the spindle between them, and by further contraction of the rays both the divergence of the daughter-chromosomes and the division of the cell-body are caused. A new condition of equilibrium is thus established in each daughter-cell until again disturbed by division of the centrosome.[2] In some cases (leucocytes) the organic radii are visible at all periods. More commonly they are lost to view by breaking up into the cell-reticulum, without, however, losing their essential relations.

No one who witnesses the operation of Heidenhain's models can fail to be impressed with its striking simulation of actual cell-division. Closer study of the facts shows, however, that the contraction-hypothesis must be considerably restricted, as has been done by the successive modifications of Hermann ('91), Drüner ('95), and others. Hermann, to whom the identification of the central spindle is due, pointed out that there is no evidence of contractility in the central spindle-fibres, which elongate instead of shorten during mitosis; and he concluded that these fibres are non-contractile supporting elements, which form a basis on which the movements of the chromosomes take place. The *mantle-fibres* are the only contractile elements in the spindle, and it is by them that the chromosomes are brought into position about the central spindle and the daughter-chromosomes are dragged apart.[3] Drüner ('95) still further restricts the hypothesis, maintaining that the progressive divergence of the spindle-poles is caused not by contraction of the astral rays ("polar fibres"), as assumed by Heidenhain (following Van Beneden and Boveri), but by an active growth or elongation of the central spindle, which goes on throughout the whole period from the earliest prophases until the close of the anaphases. This view is supported by the fact that the central spindle-fibres are always contorted during the metaphases, as if pushing against a resistance; and it harmonizes with the facts observed in the mitoses of infusorian nuclei, where no asters are present. This view has been accepted, with slight modifications, by Flemming, Boveri, Meves, Kostanecki, and also by Heidenhain. A nearly decisive argument in its favour is given by such cases as the polar bodies, or the mitosis of salamander spermatocytes as described by Meves ('96, '97, 3), where the spindle-poles are pushed out to the periphery of the cell, the polar astral rays meanwhile nearly or quite disappearing (Fig. 130). This not only strongly indicates the push of the central spindle, but also shows that the assumption of a pull by the polar rays is superfluous. But beyond this both Drüner and Meves have brought arguments against contractility in the other astral rays, endeavouring to show that these, like the spindle-fibres, are actively elongating elements, and that (Meves, '97, 3) the actual grouping of the rays during the anaphases is such as to suggest that even the division of the cell-body may be thus caused. A pushing function of the astral rays is also indicated by infolding of the nuclear membrane caused by the development of the aster as described by Platner, Watasé, Braus, Griffin, and others.[1] The contraction-hypothesis is thus restricted by Drüner and Meves to the mantle-fibres alone, though many others, among them Flemming and Kostanecki, still accept the contractility of the astral rays.

---

[1] In a modification of the apparatus devised by Rhumbler ('97), the same effect is produced without the hinges.

[2] *Cf.* p. 57. For critique of this hypothesis, see Fick ('97), Rhumbler ('96, '97), and Meves ('97, 4).

[3] Belajeff ('94) and Strasburger ('95) have accepted a similar view as applied to mitosis in plant-cells.

(*b*) *Other Facts and Theories.* — Even in the restricted form indicated above the contraction-hypothesis encounters serious difficulties, one of which is the fact urged by me in an earlier paper ('95), and subsequently by Richard Hertwig ('98), that in the eggs of echinoderms and many other dividing cells the daughter-chromosome plates, extending through the whole substance of the spindle, wander to the extreme ends of the spindle — a process which demands a contraction of the fibres almost to the vanishing point, while in point of fact not even a shortening and thickening of the fibres can be seen (Fig. 52). Moreover, in these cases, no distinction can be seen between central spindle-fibres and mantle-fibres, and we can only save the contraction-hypothesis by the improbable assumption that fibres indistinguishably mingled, and having the same mode of origin, structure, and staining-reaction, have exactly opposite functions. The inadequacy of the general theory is sufficiently apparent from the fact that in amitosis cells many divide without any amphiaster whatever. In Infusoria mitosis seems to occur in the entire absence of asters, although the cells divide by constriction, and the analogy with Heidenhain's model entirely fails.

---

[1] *Cf.* p. 68. It should be pointed out that the originator of the pushing theory was Watasé ('93), who ingeniously developed an hypothesis exactly the opposite of Van Beneden's, assuming both astral rays and spindle-fibres to be actively elongating fibres, dove-tailing in the spindle-region, and pushing the chromosomes apart. This hypothesis is, I believe, inconsistent with the phenomena observed in multiple asters and elsewhere, yet it probably contains a nucleus of truth that forms the basis of Drüner's conception of the central spindle.

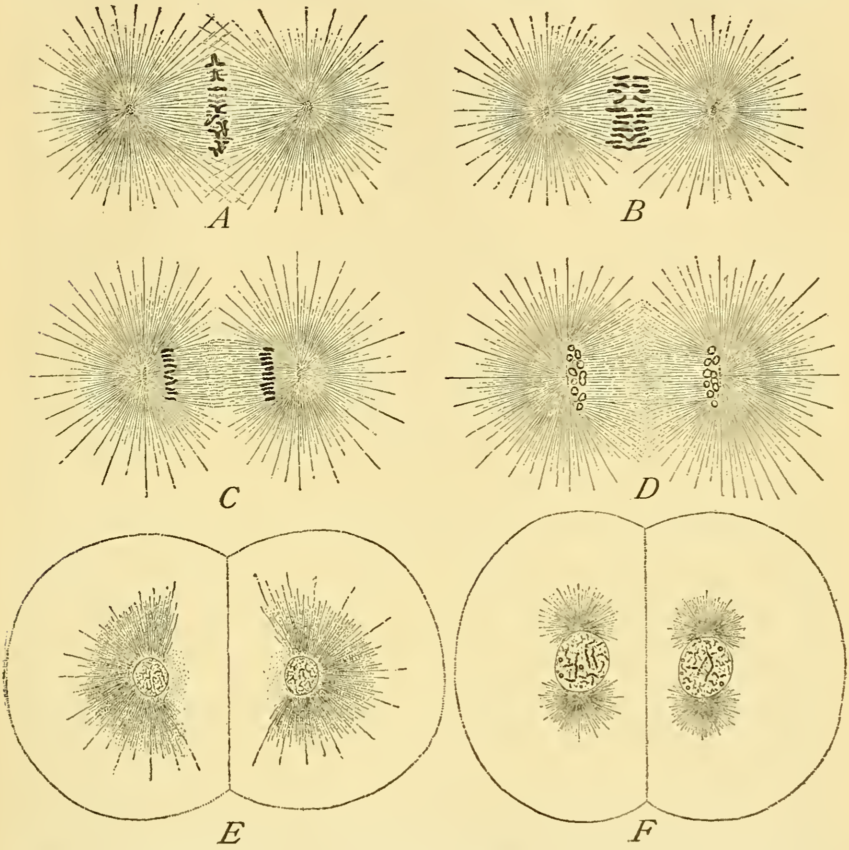

Fig. 52.—The later stages of mitosis in the egg of the sea-urchin *Toxopneustes* (*A–D*, × 1000; *E–F*, × 500).

A. Metaphase; daughter-chromosomes drawing apart but still united at one end. *B*. Daughter-chromosomes separating. *C*. Late anaphase; daughter-chromosomes lying near the spindle-poles. *D*. Final anaphase; daughter chromosomes converted into vesicles. *E*. Immediately after division, the asters undivided; the spindle has disappeared. *F*. Resting 2-cell stage, the asters divided into two in anticipation of the next division.

In Figs. *A* and *B* the centrosome consists of a mass of intensely staining granules, which in *C* and *D* elongates at right angles to the spindle-axis. In *F* the centrosome appears as a single or double granule, which in later stages gives rise to a pluricorpuscular centrum like that in *A*. The connection between *D* and *F* is not definitely determined.

In *Euglypha*, according to Schewiakoff (Fig. 39), division of the cell-body appears to take place quite independently of the mitotic figure. Again, a considerable number of cases are now known in which during the fertilization of the egg a large amphiaster is formed, with astral rays sometimes extending throughout almost the entire egg, only to disappear or become greatly reduced without the occurrence of division, the ensuing cleavage being effected by a new amphiaster or by the recrudescence of the old.[1] For these and other reasons we must admit the probability that contractility of the astral fibrillæ, if it exists, is but the expression or consequence of a more deeply lying phenomena of more general significance. The subtlety of the problem is strikingly shown by Boveri's remarkable observations on abnormal sea-urchin eggs ('96), which show (1) that the periodic division of the centrosome and formation of the amphiaster may take place independently of the nucleus; (2) that the spindle, as well as the asters, is concerned in division of the cell-body; and (3) that an amphiaster without chromosomes is unable to effect normal division of the cell-body. The first and third of these facts are shown by eggs in which during the first cleavage all of the chromatin passes to one pole of the spindle, so that one of the resulting halves of the egg receives no nucleus, but only a centrosome and aster. In this half perfect amphiasters are formed simultaneously with each cleavage in the other half, *yet no division of the protoplasmic mass occurs.*[2] The second fact is shown in polyspermic eggs, in which multipolar astral systems are formed by union of the several sperm-asters (Figs. 53, 101). In such eggs *cleavages only occur between asters that are joined by a spindle.* Normal cleavage of the cell-body thus requires the complete apparatus of mitosis, and even though the fibres be contractile they cannot fully operate in the absence of chromatin.

We may now turn to theories based on the hypothesis, first suggested by Fol in 1873, that the astral foci (*i.e.* centrosomes) represent dynamic centres of attractive or other forces. It should be noted that this hypothesis involves two distinct questions, one relating to the origin of the amphiaster, the other to its mode of action; and we have seen that some of the foremost advocates of the contraction-hypothesis, including Van Beneden and Boveri, have held the centrosomes to be attractive centres. Apart from the movements of the chromosomes, the most obvious indication that the centrosomes are dynamic centres is the extraordinary resemblance of the amphiaster to the lines of force in a magnetic field as shown by the arrangement of iron-filings about the poles of a horseshoe magnet — a resemblance pointed out by Fol himself, and urged by many later writers,[3] especially Ziegler ('95) and Gallardo ('96, '97). It is impossible to regard this analogy as exact; first, because it is inconsistent with the occurrence of tripolar astral figures; second, as Meves has recently urged [1] the course of the astral fibres does not really coincide with the lines of force, the most important deviation being the crossing of the rays opposite the equatorial region of the spindle, which is impossible in the magnetic or electric field. We must, however, remember that the amphiaster is formed in a viscid medium, that it may perform various movements, and that its fibres probably possess the power of active growth. The physical or chemical effect of the centres, through which the amphiaster primarily arises, may thus be variously disturbed or modified in later stages, and the crossing of the rays is therefore not necessarily fatal to the assumption of dynamic centres. Bütschli ('92, '98) has, moreover, recently shown that a close *simulacrum* of the amphiaster, showing a distinct crossing of the rays, may be produced in an artificial alveolar structure (coagulated gelatine) by tractive forces cen-

---

[1] *Cf.* p. 213.

[2] This result is opposed to Boveri's earlier work on *Ascaris* (p. 355), and is modified by Ziegler ('98), who observed in a single case that an irregular cleavage occurred in the enucleated half after two or three divisions of the centrosome. On the other hand, it is supported by Morgan's convincing experiments on the eggs of *Arbacia* (p. 308).

[3] *Cf.* the interesting photographic figures of Ziegler ('95). A still closer *simulacrum* of the amphiaster is produced by fine crystals of sulphate of quinine (a semiconductor) sus-

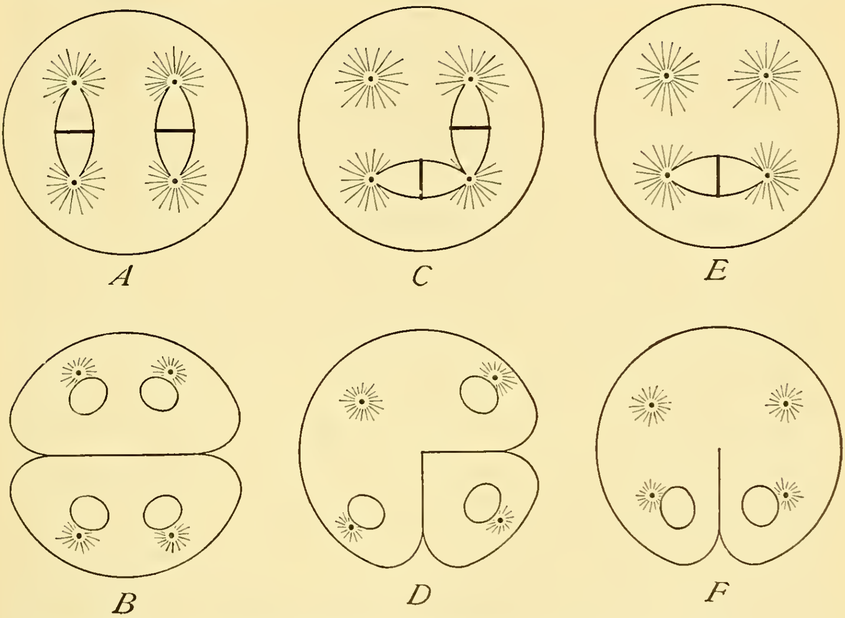

Fig. 53. — Division of dispermic eggs in sea-urchin eggs, schematic. [BOVERI.]
A. C. E. Eggs before division, showing various connections of the asters. *B. D. F.* Resulting division in the three respective cases, showing cleavage only between centres connected by a spindle.

---

pended in spirits of turpentine (a poor conductor) between two electric poles. This experiment, devised by Faraday, has recently been applied by Gallardo ('96, '97) to an analysis of the mitotic figure.

[1] '96, p. 371.

tring in two adjacent points. This result is obtained by warming and then cooling a film of thick gelatine-solution, filled with air-bubbles, and then coagulating the mass in chromic acid. Such a film shows a fine alveolar structure, which assumes a radial arrangement about the air-bubbles, owing to the traction exerted on the surrounding structure by shrinkage of the bubbles on cooling. The amphiastral *simulacra* are produced about two adjacent bubbles, — a "spindle" being formed between them, and the "astral rays" sometimes showing a crossing like that seen in the actual amphiaster (Bütschli is himself unable to explain fully how the crossing arises). The protoplasmic asters are maintained by Bütschli to be, in like manner, no more than a radial configuration of the alveolar cell-substance caused by centripetal diffusion-currents toward the astral centres.[1] The most interesting part of this view is the assumption that these currents are caused by *specific chemical changes taking place in the centrosome* which causes an absorption of liquid from the surrounding region. "The astral bodies are structures which, under certain circumstances, function in a measure as centres from which emanate chemical actions upon protoplasm and nucleus; and the astral phenomena which appear about the centrosomes are only a result incidental to this action of the central bodies upon the plasma."[2] Through centripetal currents thus caused arise the asters, and they may even account, in a measure, for the movements of the chromosomes.[3] This latter part of Bütschli's conception is, I believe, quite inadequate; but the hypothesis of definite chemical activity in the centrosome is a highly important one, which is sustained by the staining-reactions of the centrosome and by its definite morphological changes during the cycle of cell-division.

More or less similar chemical hypotheses have been suggested by several other writers.[4] Of these perhaps the most interesting is Strasburger's suggestion,[5] that the movements of the chromosomes may be of a chemotactic character, which I suspect may prove to have been one of the most fruitful contributions to the subject. Beside this may be placed Carnoy's still earlier hypothesis ('85), that the asters are formed under the influence of specific *ferments* emanating from the poles of the nucleus. Mathews ('99, 2) has recently pointed out that there is a considerable analogy between the formation of the astral rays and that of fibrin-fibrils under the influence of fibrin-ferment, adding the suggestion that the centrosome may actually contain fibrin-ferment. Attention may be called here to the fact, now definitely determined by experiment,[1] that cell-division may be incited by chemical stimulus. In most of the cases thus far experimentally examined the divisions so caused are pathological in character, but in others they are quite normal, as shown in Loeb's remarkable results on the production of parthenogenesis in sea-urchin eggs by chemical stimulus, as described at pages 215 and 308. While these experiments by no means show that division is itself merely a chemical process, they strongly suggest that it cannot be adequately analyzed without reckoning with the chemical changes involved in it.

---

[1] Carnoy ('85) and Platner ('86) had previously held a similar view, suggesting that not only the spindle-formation, but also the movements of the chromosomes, might be explained as the result of protoplasmic currents.

[2] '92, 1, p. 538.

[3] '92, 2, p. 160; '92, 3, p. 10.

[4] *Cf.* the first edition of this work, p. 77, also Ziegler ('95).

[5] '93, 2.

Résumé. A review of the foregoing facts and theories shows how far we still are from any real understanding of the process involved either in the origin or in the mode of action of the mitotic figure. The evidence seems well-nigh demonstrative, in case of the mantle-fibres and the astral rays, that Van Beneden's hypothesis contains an element of truth, but we must now recognize that it was formulated in too simple a form for the solution of so complex a problem. No satisfactory hypothesis can, I believe, be reached that does not reckon with the chemical changes occurring at the spindle-poles and in the nucleus; and these changes are probably concerned not only with the origin of the amphiaster, but also with the movements of the chromosomes. In cases where the centrosome persists from cell to cell we may perhaps regard it as the vehicle of specific substances (ferments?) which become active at the onset of mitosis, and run through a definite cycle of changes, to initiate a like cycle in the following generation; and it is quite conceivable that such substances may persist at the nuclear poles, or may be re-formed there as an after-effect, even though the formed centrosome disappears.[2] In this consideration we may find a clue to the strange fact — should it indeed prove to be a fact — that the centrosome may divide, yet afterward disappear without discoverable connection with the centrosomes of the succeeding mitosis, as several recent observers have maintained.[3] When all is said, we must admit that the mechanism of mitosis in every phase still awaits adequate physiological analysis. The suggestive experiments of Bütschli and Heidenhain lead us to hope that a partial solution of the problem may be reached along the lines of physical and chemical experiment. At present we can only admit that none of the conclusions thus far reached, whether by observation or by experiment, are more than the first *naive* attempts to analyze a group of most complex phenomena of which we have little real understanding.

---

[1] See pp. 306, 308.

[2] *Cf.* p. 215.

[3] *Cf.* p. 213.

2. *Division of the Chromosomes*

In developing his theory of fibrillar contractility, Van Beneden expressed the view — only, however, as a possibility — that the splitting of the chromosomes might be passively caused by the contractions of the two sets of opposing spindle-fibres to which each is attached.[1] Later observations have demonstrated that this suggestion cannot be sustained; for in many cases the chromatin-thread splits before division of the centrosome and the formation of the achromatic figure — sometimes during the spireme-stage, or even in the reticulum, while the nuclear membrane is still intact. Boveri showed this to be the case in *Ascaris*, and a similar fact has been observed by many observers since, both in plants and in animals.

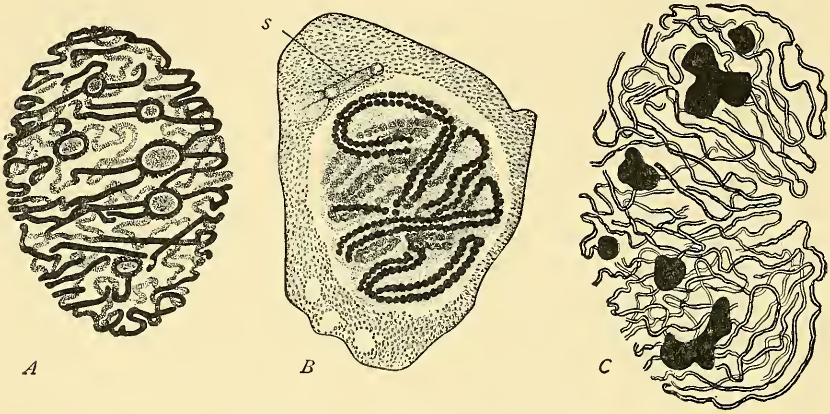

Fig. 54. — Nuclei in the spireme-stage.

A. From the endosperm of the lily, showing true nucleoli. [FLEMMING.]

B. Spermatocyte of salamander. Segmented double spireme-thread composed of chromomeres and completely split. Two centrosomes and central spindle at *s*. [HERMANN.]

C. Spireme-thread completely split, with six nucleoli. Endosperm of *Fritillaria*. [FLEMMING.]

The splitting of the chromosomes is therefore, in Boveri's words, "*an independent vital manifestation, an act of reproduction on the part of the chromosomes.*"[2]

All of the recent researches in this field point to the conclusion that this act of division must be referred to the fission of the chromatin-granules or chromomeres of which the chromatin-thread is built. These granules were first clearly described by Balbiani ('76) in the chromatin-network of epithelial cells in the insect-ovary, and he found that the spireme-thread arose by the linear arrangement of these granules in a single row like a chain of bacteria.[3] Six years later Pfitzner ('82) added the interesting discovery that during the mitosis of various tissue-cells of the salamander, the granules of the spireme-thread *divide by fission and thus determine the longitudinal splitting of the entire chromosome.* This discovery was confirmed by Flemming in the following year ('82, p. 219), and a similar result has been reached by many other observers (Fig. 54). The division of the chromatin-granules may take place at a very early period. Flemming observed as long ago as 1881 that the chromatin-thread might split in the spireme-stage (epithelial cells of the salamander), and this has since been shown to occur in many other cases; for instance, by Guignard in the mother-cells of the pollen in the lily ('91). Brauer's recent work on the spermatogenesis of *Ascaris* shows that the fission of the chromatin-granules here takes place even before the spireme-stage, when the chromatin is still in the form of a reticulum, and long before the division of the centrosome (Fig. 55). He therefore concludes: "With Boveri I regard the splitting as an

---

[1] '87, p. 279.

[2] '88, p. 113.

[3] See '81, p. 638.

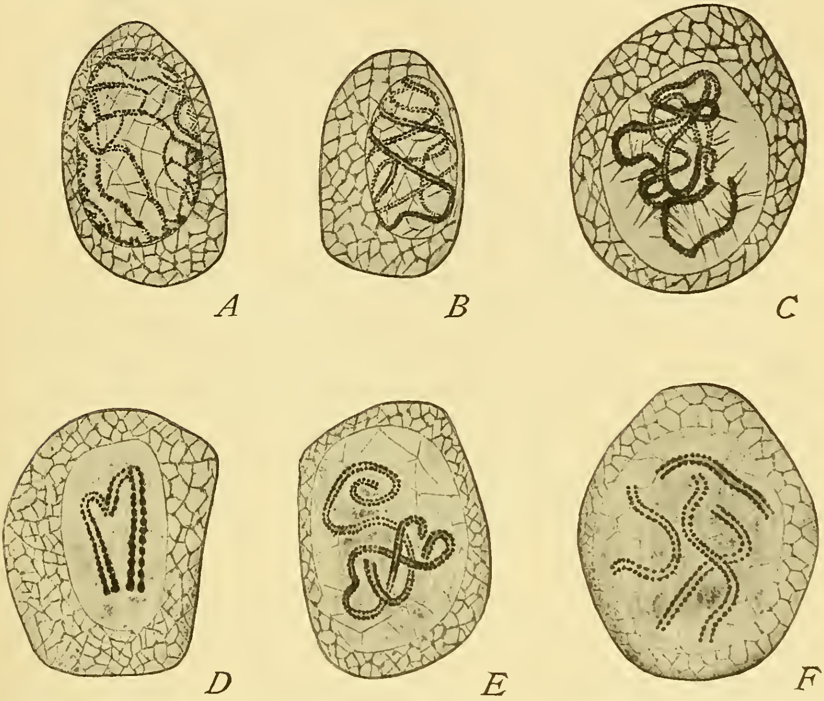

Fig. 55. — Formation of chromosomes and early splitting of the chromatin-granules in spermatogonia of *Ascaris megalocephala*, var. *bivalens*. [BRAUER.]

A. Very early prophase; granules of the nuclear recticulum already divided. *B*. Spireme; the continuous chromatin-thread split throughout. *C*. Later spireme. *D*. Shortening of the thread. *E*. Spireme-thread divided into two parts. *F*. Spireme-thread segmented into four split chromosomes.

independent reproductive act of the chromatin. The reconstruction of the nucleus, and in particular the breaking up of the chromosomes after division into small granules and their uniform distribution through the nuclear cavity, is, in the first place, for the purpose of allowing a uniform growth to take place; and in the second place, after the granules have grown to their normal size, *to admit of their precisely equal quantitative and qualitative division.* I hold that all the succeeding phenomena, such as the grouping of the granules in threads, their union to form larger granules, the division of the thread into segments and finally into chromosomes, are of secondary importance; all these are only for the purpose of bringing about in the simplest and most certain manner the transmission of the daughter-granules (Spalthälften) to the daughter-cells."[1] "In my opinion the chromosomes are not independent individuals, but only groups of numberless minute chromatin-granules, which alone have the value of individuals."[2]

These observations certainly lend strong support to the view that the chromatin is to be regarded as a morphological aggregate — as a congeries or colony of self-propagating elementary organisms capable of assimilation, growth, and division. They prove, moreover, that mitosis involves two distinct though closely related factors, one of which is the fission of the chromatic nuclear substance, while the other is the distribution of that substance to the daughter-cells. In the first of these it is the chromatin that takes the active part; in the second it would seem that the main *rôle* is played by the amphiaster.

E. DIRECT OR AMITOTIC DIVISION

1. *General Sketch*

We turn now to the rarer and simpler mode of division known as amitosis; but as Flemming has well said, it is a somewhat trying task to give an account of a subject of which the final outcome is so unsatisfactory as this; for in spite of extensive investigation, we still have no very definite conclusion in regard either to the mechanism of amitosis or its biological meaning. Amitosis, or direct division, differs in two essential respects from mitosis. First, the nucleus remains in the resting state (reticulum), and there is no formation of a spireme or of chromosomes. Second, division occurs without the formation of an amphiaster; hence the centrosome is not concerned with the nuclear division, which takes place by a simple constriction. The nuclear substance, accordingly, undergoes a division of its total *mass*, but not of its individual elements or chromatin-granules (Fig. 56).

---

[1] '93, pp. 203, 204.

[2] *l.c.*, p. 205.

Before the discovery of mitosis, nuclear division was generally assumed to take place in accordance with Remak's scheme (p. 63). The rapid extension of our knowledge of mitotic division between the years 1875 and 1885 showed, however, that such a mode of division was, to say the least, of rare occurrence, and led to doubts as to whether it ever actually took place as a normal process. As soon, however, as attention was especially directed to the subject, many cases of amitotic division were accurately determined, though very few of them conformed precisely to Remak's scheme. One such case is that described by Carnoy in the follicle-cells of the egg in the mole-cricket, where division begins in the fission of the nucleolus, followed by that of the nucleus. Similar cases have been since described, by Hoyer ('90) in the intestinal epithelium of the nematode *Rhabdonema*, by Korschelt in the intestine of the annelid *Ophryotrocha*, and in a few other cases. In many cases, however, no preliminary fission of the nucleolus occurs; and Remak's scheme must, therefore, be regarded as one of the rarest forms of cell-division (!).

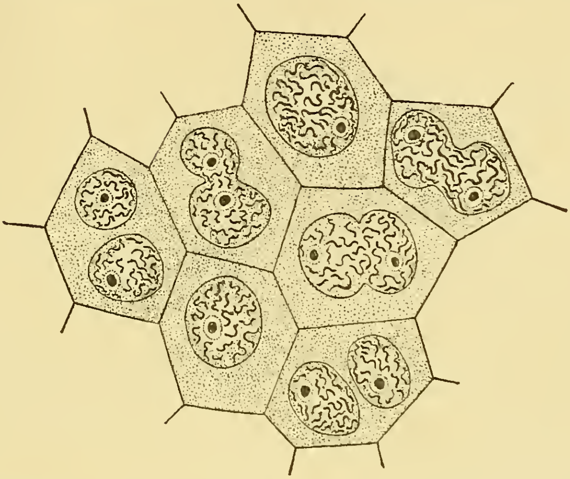

Fig. 56. — Group of cells with amitotically dividing nuclei; ovarian follicular epithelium of the cockroach. [WHEELER.]

2. *Centrosome and Attraction-sphere in Amitosis*

The behaviour of the centrosome in amitosis forms an interesting question on account of its bearing on the mechanics of cell-division. Flemming observed ('91) that the nucleus of leucocytes might in some cases divide directly without the formation of an amphiaster, the attraction-sphere remaining undivided meanwhile. Heidenhain showed in the following year, however, that in some cases leucocytes containing two nuclei (doubtless formed by amitotic division) might also contain two asters connected by a spindle. Both Heidenhain and Flemming drew from this the conclusion that direct division of the *nucleus* is in this case independent of the centrosome, but that the latter might be concerned in the division of the cell-body, though no such process was observed. A little later, however, Meves published remarkable observations that seem to indicate a functional activity of the attraction-sphere during amitotic nuclear division in the "spermatogonia" of the salamander.[1] Krause and Flemming observed that in the autumn many of these cells show peculiarly lobed and irregular nuclei (the "polymorphic nuclei" of Bellonci). These were, and still are by some writers, regarded as degenerating nuclei. Meves, however, asserts — and the accuracy of his observations is in the main vouched for by Flemming — that in the ensuing spring these nuclei become uniformly rounded, and may then divide amitotically. In the autumn the attraction-sphere is represented by a diffused and irregular granular mass, which more or less completely surrounds the nucleus. In the spring, as the nuclei become rounded, the granular substance draws together to form a definite rounded sphere, in which a distinct centrosome may sometimes be made out. Division takes place in the following extraordinary manner: The nucleus assumes a dumb-bell shape, while the attraction-sphere becomes drawn out into a band which surrounds the central part of the nucleus, and finally forms a closed ring, encircling the nucleus. After this the nucleus divides into two, while the ring-shaped attraction-sphere ("archoplasm") is again condensed into a sphere. The appearances suggest that the ring-shaped sphere actually compresses the nucleus and cuts it through. In a later paper ('94) Meves shows that the diffused "archoplasm" of the autumn-stage arises by the breaking down of a definite spherical attraction-sphere, which is re-formed again in the spring in the manner described, and in this condition the cells may divide *either mitotically or amitotically*. He adds the interesting observation, since confirmed by Rawitz ('94), that in the spermatocytes of the salamander the attraction-spheres of adjoining cells are often connected by intercellular bridges, but the meaning of this has not yet been determined.

It is certain that the remarkable transformation of the sphere into a ring during amitosis is not of universal, or even of general, occurrence, as shown by the later studies of Vom Rath ('95, 3). In leucocytes, for example, the sphere persists in its typical form, and contains a centrosome, during every stage of the division; but it is an interesting fact that during all these stages the sphere lies on the concave side of the nucleus in the bay which finally cuts through the entire nucleus. Again, in the liver-cells of the isopod *Porcellio*, the nucleus divides, not by constriction, as in the leucocyte, but by the appearance of a nuclear plate, in the formation of which the attraction sphere is apparently not concerned.[2] The relations of the centrosome and archoplasm in amitosis are, therefore, still in doubt; but, on the whole, the evidence goes to show that they take no essential part in the process.

3. *Biological Significance of Amitosis*

A survey of the known cases of amitosis brings out the following significant facts. It is of extreme rarity, if indeed it ever occurs in embryonic cells or such as are in the course of rapid and continued multiplication. It is frequent in pathological growths and in cells such as those of the vertebrate decidua, of the embryonic envelopes of insects, or the yolk-nuclei (periblast, etc.), *which are on the way toward degeneration.* In many cases, moreover, direct nuclear division is not followed by fission of the cell-body, so that multinuclear cells and polymorphic nuclei are thus often formed. These and many similar facts led Flemming in 1891 to express the opinion that so far as the higher plants and animals are concerned amitosis is "a process which does not lead to a new production and multiplication of cells, but wherever it occurs represents either a degeneration or an aberration, or perhaps in many cases (as in the formation of multinucleated cells by fragmentation) is tributary to metabolism through the increase of nuclear surface."[1] In this direction Flemming sought an explanation of the fact that leucocytes may divide either mitotically or amitotically (*t.* Peremeschko, Löwit, Arnold, Flemming). In the normal lymph-glands, where new leucocytes are continually regenerated, mitosis is the prevalent mode. Elsewhere (wandering-cells) both processes occur. "Like the cells of other tissues the leucocytes find their normal physiological origin (Neubildung) in mitosis; only those so produced have the power to live on and reproduce their kind through the same process."[1] Those that divide amitotically are on the road to ruin. Amitosis in the higher forms is thus conceived as a purely secondary process, not a survival of a primitive process of direct division from the Protozoa, as Strasburger ('82) and Waldeyer ('88) had conceived it.

---

[1] '91, p. 628.

[2] Such a mode of amitotic division was first described by Sabatier in the crustacea ('89), and a similar mode has been observed by Carnoy and Van der Stricht.

This hypothesis has been carried still further by Ziegler and Vom Rath ('91). In a paper on the origin of the blood in fishes, Ziegler ('87) showed that the periblast-nuclei in the egg of fishes divide amitotically, and he was thus led like Flemming to the view that amitosis is connected with a high specialization of the cell and may be a forerunner of degeneration. In a second paper ('91), published shortly after Flemming's, he points out the fact that amitotically dividing nuclei are usually of large size and that the cells are in many cases distinguished by a specially intense secretory or assimilative activity. Thus, Rüge ('90) showed that the absorption of degenerate eggs in the Amphibia is effected by means of leucocytes which creep into the egg-substance. The nuclei of these cells become enlarged, divide amitotically, and then frequently degenerate. Other observers (Korschelt, Carnoy) have noted the large size and amitotic division of the nuclei in the ovarian follicle-cells and nutritive cells surrounding the ovum in insects and Crustacea. Chun found in the entodermic cells of the radial canals of siphonophores huge cells filled with nests of nuclei amitotically produced, and suggested ('90) that the multiplication of nuclei was for the purpose of increasing the nuclear surface as an aid to metabolic interchanges between nucleus and cytoplasm. Amitotic division leading to the formation of multinuclear cells is especially common in gland-cells. Thus, Klein has described such divisions in the mucous skin-glands of Amphibia, and more recently Vom Rath has carefully described it in the huge gland-cells (probably salivary) of the isopod *Anilocra* ('95). Many other cases are known. Dogiel ('90) has observed exceedingly significant facts in this field that place the relations between mitosis and amitosis in a clear light. It is a well-known fact that in stratified epithelium new cells are continually formed in the deeper layers to replace those cast off from the superficial layers. Dogiel finds in the lining of the bladder of the mouse that the nuclei of the superficial cells, which secrete the mucus covering the surface, regularly divide amitotically, giving rise to huge multinuclear cells, which finally degenerate and are cast off. The new cells that take their place are formed in the deeper layers by mitosis alone. Especially significant, again, is the case of the ciliate Infusoria, which possess two kinds of nuclei in the same cell, a macronucleus and a micronucleus. The former is known to be intimately concerned with the processes of metabolism (*cf.* p. 342). During conjugation the macronucleus degenerates and disappears and a new one is formed from the micronucleus or one of its descendants. The macronucleus is therefore essentially metabolic, the micronucleus generative in function. In view of this contrast it is a significant fact that while both nuclei divide during the ordinary process of fission the mitotic phenomena are as a rule less clearly marked in the macronucleus than in the micronucleus, and in some cases the former appears to divide directly while the latter always goes through a process of mitosis.

---

[1] '91, 2, p. 291.

These conclusions received a very important support in the work of Vom Rath on amitosis in the testis ('93). On the basis of a comparative study of amitosis in the testis-cells of vertebrates, mollusks, and arthropods he concludes that amitosis never occurs in the sperm-producing cells (spermatogonia, etc.), but only in the supporting cells (Randzellen, Stützzellen). The former multiply through mitosis alone. The two kinds of cells have, it is true, a common origin in cells which divide mitotically. When, however, they have once become differentiated, they remain absolutely distinct; amitosis never takes place in the series which finally results in the formation of spermatozoa, and the amitotically dividing "supporting-cells" sooner or later perish. Vom Rath thus reached the remarkable conclusion that "when once a cell has undergone amitotic division it has received its death-warrant; it may indeed continue for a time to divide by amitosis, but inevitably perishes in the end."[1]

---

[1] '91, p. 331.

There is, however, strong evidence that this conclusion is too extreme. Meves ('94) has given good reason for the conclusion that in the salamander the nuclei of the sperm-producing cells (spermatogonia) may divide by amitosis yet afterward undergo normal mitotic division, and Preusse ('95) has reached a similar result in the case of insect-ovaries. Perhaps the most convincing evidence in this direction is afforded by Pfeffer's ('99) recent experiments on *Spirogyra*. If this plant be placed in water containing 0.5 to 1.0% of ether, active growth and division continue, but only by amitosis. If, however, the same individuals be replaced in water, *mitotic division is resumed* and entirely normal growth continues. This seems to show conclusively that amitosis, in lower forms of life at least, does not necessarily mean the approach of degeneration, but is a result of special conditions. Nevertheless, there can be no doubt that Flemming's hypothesis in a general way represents the truth, and that in the vast majority of cases amitosis is a secondary process which does not fall in the generative series of cell-divisions.

F. Summary and Conclusion

All cells arise by division from preëxisting cells, cell-body from cell-body, nucleus from nucleus, plastids (when these bodies are present) from plastids, and in some cases centrosomes from centrosomes. The law of genetic continuity thus applies not merely to the cell considered as a whole, but also to some of its structural constituents.

In mitosis, the usual and typical mode of division, the nucleus undergoes a complicated transformation, and, together with some of the cytoplasmic material, gives rise to the *mitotic figure*. Of this, the most characteristic features are the *chromatic figure*, consisting of chromosomes derived from the chromatin, and the *achromatic figure*, derived from the cytoplasm, the nucleus, or from both, and consisting of a spindle, at each pole of which, as a rule, is a centrosome and aster. There is, however, strong evidence that both these latter structures may in some cases be wanting, and the spindle is therefore probably to be regarded as the most essential element.

The chromosomes, always of the same number in a given species (with only apparent exceptions), arise by the transformation of the chromatin-reticulum into a thread which breaks into segments and splits lengthwise throughout its whole extent. The two halves are thereupon transported in opposite directions along the spindle to its respective poles and there enter into the formation of the two corresponding daughter-nuclei. The spireme-thread, and hence the chromosome, arises from a single series of chromatin-granules or chromomeres which, by their fission, cause the splitting of the thread.

Every individual chromatin-granule therefore contributes its quota to each of the daughter-nuclei, but it is uncertain whether they are persistent bodies or only temporary structures like the chromosomes themselves.

The spindle may arise from the achromatic substance of the nucleus, from the cytoplasmic substance, or from both. When centrosomes are present it is they, as a rule, that lead the way in division. About the daughter-centrosomes as foci are formed the asters and between them stretches the spindle, forming an *amphiaster* which is the most highly developed form of the achromatic figure. When centrosomes are absent, as now appears to be the case in the higher plants, the spindle is formed from fibrous protoplasmic elements that gradually group themselves into a spindle.

The mechanism of mitosis is imperfectly understood. Experimental studies give ground for the conclusion that the changes undergone by the chromatic and the achromatic figures respectively are parallel but in a measure independent processes, which are however so correlated that both must coöperate for complete cell-division. Thus there is strong evidence that the fission of the chromatin-granules, and the splitting of the thread, is not caused by division of the centrosome or the formation of the spindle, but only accompanies it as a parallel phenomenon. The divergence of the daughter-chromosomes, on the other hand, is in some manner determined by the spindle-fibres. There are cogent reasons for the view that some of these fibres are contractile elements which, like muscle-fibres, drag the daughter-chromosomes asunder; while other spindle-fibres act as supporting and guiding elements, and probably by their elongation push the spindle-poles apart. The adequacy of this explanation is, however, doubtful, and it is not improbable that the centrosome or spindle-poles are centres of chemical or other physiological activities that play an essential part in the process and are correlated with those taking place in the chromatin. The functions of the astral rays are likewise still involved in doubt, the rays being regarded by some investigators as contractile elements like muscle-fibres, by others as rigid supporting fibres, or even as actively pushing elements like those of the central spindle. It is generally believed further that they play a definite part in division of the cell-body — a conclusion supported by the fact that the size of the aster is directly related to that of the resulting cell. On the other hand division of the cell-body may apparently occur in the absence of asters (as in amitosis, or among the Infusoria).

These facts show that mitosis is due to the coördinate play of an extremely complex system of forces which are as yet scarcely comprehended. Its general significance is, however, obvious. *The effect* *of mitosis is to produce a meristic division, as opposed to a mere mass-division, of the chromatin of the mother-cell, and its equal distribution to the nuclei of the daughter-cells.* To this result all the operations of mitosis are tributary; and it is a significant fact that this process is characteristic of all embryonic and actively growing cells, while mass-division, as shown in amitosis, is equally characteristic of highly specialized or degenerating cells in which development is approaching its end.

LITERATURE. II[1]

Auerbach, L. — Organologische Studien. *Breslau*, 1874.

Van Beneden, E. — Recherches sur la maturation de l'œuf, la fécondation et la division cellulaire: *Arch. de Biol.*, IV. 1883.

Van Beneden and Neyt. — Nouvelles recherches sur la fécondation et la division mitosque chez l'Ascaride mégalocephale: *Bull. Acad. roy. de Belgique*, III. 14. No. 8. 1887.

Boveri, Th. — Zellenstudien: I. *Jena. Zeitschr.*, XXI. 1887; II. *Ibid.* XXII. 1888; III. *Ibid.* XXIV. 1890.

Drüner, L. — Studien über den Mechanismus der Zelltheilung. *Jena. Zeitschr.*, XXIX., II. 1894.

Erlanger, R. von. — Die neuesten Ansichten über die Zelltheilung und ihre Mechanik: *Zoöl. Centralb.*, III. 2. 1896.

Id. — Über die Befruchtung und erste Teilung des Ascariseies: *Arch. mik. Anat.*, XLIX. 1897.

Flemming, W., '92. — Entwicklung und Stand der Kenntnisse über Amitose: *Merkel und Bonnet's Ergebnisse*, II. 1892.

Id. — Zelle. (See Introductory list. Also general list.)

Fol, H. — (See List IV.)

Heidenhain, M. — Cytomechanische Studien: *Arch. f. Entwickmech.*, I. 4. 1895.

Id. — Neue Erläuterungen zum Spannungsgesetz der centrirten Systeme: *Morph. Arb.*, VII. 1897.

Hermann, F. — Beitrag zur Lehre von der Entstehung der karyokinetischen Spindel: *Arch. mik. Anat.*, XXXVII. 1891.

Hertwig, R. — Über Centrosoma und Centralspindel: *Sitz.-Berg. Ges. Morph. und Phys. München*, 1895, Heft I.

Kostanecki and Siedlecki. — Über das Verhalten der Centrosomen zum Protoplasma: *Arch. mik. Anat.*, XLVIII. 1896.

Mark, E. L. — (See List IV.)

Meves, Fr. — Zellteilung: *Merkel und Bonnet's Ergebnisse*, VI. 1897.

Reinke, F. — Zellstudien: I. *Arch. mik. Anat.*, XLIII. 1894; II. *Ibid.* XLIV. 1894.

Strasburger, E. — Karyokinetische Probleme: *Jahrb. f. Wiss. Botan.*, XXVIII. 1895.

Strasburger, Osterhout, Mottier, and Others. — Cytologische Studien aus dem Bonner Institut: *Jahrb. wiss. Bot.*, XXX. 1897.

Waldeyer, W. — Über Karyokinese und ihre Beziehungen zu den Befruchtungsvorgängen: *Arch. mik. Anat.*, XXXII. 1888. *Q.J.M.S.*, XXX. 1889–90.

---

[1] See also Literature, IV., p. 231.

CHAPTER III

THE GERM-CELLS

"Not all the progeny of the primary impregnated germ-cells are required for the formation of the body in all animals; certain of the derivative germ-cells may remain unchanged and become included in that body which has been composed of their metamorphosed and diversely combined or confluent brethren; so included, any derivative germ-cell may commence and repeat the same processes of growth by imbibition and of propagation by spontaneous fission as those to which itself owed its origin; followed by metamorphoses and combinations of the germ-masses so produced, which concur to the development of another individual."
RICHARD OWEN.[1]

"Es theilt sich demgemäss das befruchtete Ei in das Zellenmaterial des Individuums und in die Zellen für die Erhaltung der Art."
M. NUSSBAUM.[2]

THE germ from which every living form arises is a single cell, derived by the division of a parent-cell of the preceding generation. In the unicellular plants and animals this fact appears in its simplest form as the fission of the entire parent-body to form two new and separate individuals like itself. In all the multicellular types the cells of the body sooner or later become differentiated into two groups, which as a matter of practical convenience may be sharply distinguished from one another. These are, to use Weismann's terms: (1) the *somatic cells*, which are differentiated into various tissues by which the functions of individual life are performed and which collectively form the "body," and (2) the *germ-cells*, which are of minor significance for the individual life and are destined to give rise to new individuals by detachment from the body. It must, however, be borne in mind that the distinction between germ-cells and somatic cells is not absolute, as some naturalists have maintained, but only relative. The cells of both groups have a common origin in the parent germ-cell; both arise through mitotic cell-division during the cleavage of the ovum or in the later stages of development; both have essentially the same structure and both *may* have the same power of development, for there are many cases in which a small fragment of the body consisting of only a few somatic cells, perhaps only of one, may give rise by regeneration to a complete body. The distinction between somatic and germ-cells is an expression of the physiological division of labour; and while it is no doubt the most fundamental and important differentiation in the multicellular body, it is nevertheless to be regarded as differing only in degree, not in kind, from the distinctions between the various kinds of somatic cells.

---

[1] *Parthenogenesis*, p. 3, 1849.

[2] *Arch. Mik. Anat.*, XVIII., p. 112, 1880.

In the lowest multicellular forms, such as *Volvox* (Fig. 57), the differentiation appears in a very clear form. Here the body consists of a hollow sphere, the walls of which consist of two kinds of cells. The very numerous smaller cells are devoted to the functions of nutrition and locomotion, and sooner or later die. A number, usually eight, of larger cells are set aside as germ-cells, each of which by progressive fission may form a new individual like the parent. In this case the germ-cells are simply scattered about among the somatic cells, and no special sexual organs exist. In all the higher types the germ-cells are more or less definitely aggregated in groups, supported and nourished by somatic cells specially set apart for that purpose and forming distinct sexual organs, the *ovaries* and *spermaries* or their equivalents. Within these organs the germ-cells are carried, protected, and nourished; and here they undergo various differentiations to prepare them for their future functions.

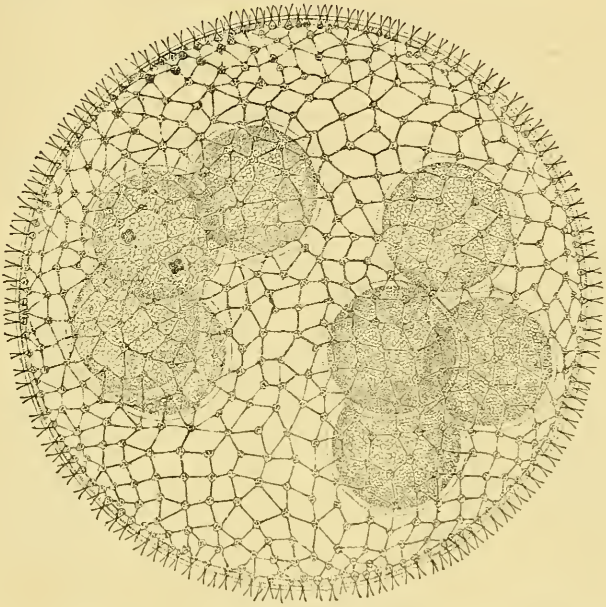

Fig. 57. — *Volvox*, showing the small ciliated somatic cells and eight large germ-cells (drawn from life by J. H. EMERTON).

In the earlier stages of embryological development the progenitors of the germ-cells are exactly alike in the two sexes and are indistinguishable from the surrounding somatic cells. As development proceeds, they are first differentiated from the somatic cells and then diverge very widely in the two sexes, undergoing remarkable transformations of structure to fit them for their specific functions. The structural difference thus brought about between the germ-cells is, however, only the result of physiological division of labour. The female germ-cell, or ovum, supplies most of the material for the body of the embryo and stores the food by which it is nourished. It is therefore very large, contains a great amount of cytoplasm more or less laden with food-matter (*yolk* or *deutoplasm*), and in many cases becomes surrounded by membranes or other envelopes for the protection of the developing embryo. On the whole, therefore, the early life of the ovum is devoted to the accumulation of cytoplasm and the storage of potential energy, and its nutritive processes are largely constructive or anabolic. On the other hand, the male germ-cell or spermatozoön contributes to the mass of the embryo only a very small amount of substance, comprising as a rule only a single nucleus and a very small quantity of cytoplasm. It is thus relieved from the drudgery of making and storing food and providing protection for the embryo, and is provided with only sufficient cytoplasm to form a locomotor apparatus, usually in the form of one or more cilia, by which it seeks the ovum. It is therefore very small, performs active movements, and its metabolism is characterized by the predominance of the destructive or katabolic processes by which the energy necessary for these movements is set free.[1] When finally matured, therefore, the ovum and spermatozoön have no external resemblance; and while Schwann recognized, though somewhat doubtfully, the fact that the ovum is a cell, it was not until many years afterward that the spermatozoön was proved to be of the same nature.

A. The Ovum

The animal egg (Figs. 58–59) is a huge spheroidal cell, sometimes naked, but more commonly surrounded by one or more membranes which may be perforated by a minute opening, the *micropyle*, through which the spermatozoön enters (Fig. 63). It contains an enormous nucleus known as the *germinal vesicle*, within which is a very conspicuous nucleolus known to the earlier observers as the *germinal spot*. In many eggs the latter is single, but in other forms many nucleoli are present, and they are sometimes of more than one kind, as in tissue-cells.[1] In many forms no centrosome or attraction-sphere is found in the egg until the initial stages in the formation of the polar bodies, though Mertens ('93) describes a centrosome and attraction-sphere in the young ovarian eggs of a number of vertebrates (Fig. 79), while Platner ('89) and Stauffacher ('93) find what they believe to be centrosomes in much later stages of *Aulostomum* and *Cyclas*, lying outside the nuclear membrane. Beside these cases should be placed those described by Balbiani, Munson, Nemec, and others in which a body closely resembling an attraction-sphere is identified as a "yolk-nucleus" or "vitelline body," as described at page 158. In none of these cases is the identification of this body wholly satisfactory, nor is it known to have any connection with the polar mitoses. Most observers find no centrosome until the prophases of the first polar mitosis. Its origin is still problematical, some observers believing it to arise *de novo* in the cytoplasm (Mead), others concluding that it is of nuclear origin (Mathews, Van der Stricht, Rückert), still others that it persists in the cytoplasm hidden among the granules. In any case it is again lost to view after formation of the polar bodies, to be replaced by the cleavage-centrosomes which arise in connection with the spermatozoön (p. 187).

---

[1] The metabolic contrast between the germ-cells has been fully discussed in a most suggestive manner by Geddes and Thompson in their work on the *Evolution of Sex;* and these authors regard this contrast as but a particular manifestation of a metabolic contrast characteristic of the sexes in general.

The egg-cytoplasm almost always contains a certain amount of nutritive matter, the *yolk* or *deutoplasm*, in the form of liquid drops, solid spheres or other bodies suspended in the meshwork and varying greatly in different cases in respect to amount, distribution, form, and chemical composition.

1. *The Nucleus*

The nucleus or germinal vesicle occupies at first a central or nearly central position, though it shows in some cases a distinct eccentricity even in its earliest stages. As the growth of the egg proceeds, the eccentricity often becomes more marked, and the nucleus may thus come to lie very near the periphery. In some cases, however, the peripheral movement of the germinal vesicle occurs only a very short time before the final stages of maturation, which may coincide with the time of fertilization. Its form is typically that of a spherical sac, surrounded by a very distinct membrane (Fig. 58); but during the growth of the egg it may become irregular or even amœboid (Fig. 77), and, as Korschelt has shown in the case of insect-eggs, may move through the cytoplasm toward the source of food. Its structure is on the whole that of a typical cell-nucleus, but is subject to very great variation, not only in different animals, but also in different stages of ovarian growth. Sometimes, as in the echinoderm ovum, the chromatin forms a beautiful and regular reticulum consisting of numerous chromatin-granules suspended in a network of linin (Fig. 58). In other cases, no true reticular stage exists, the nucleus containing throughout the whole period of its growth the separate daughter-chromosomes of the preceding division (copepods, selachians, Amphibia),[1] and these chromosomes may undergo the most extraordinary changes of form, bulk, and staining-reaction during the growth of the egg.[2] It is a very interesting and important fact that during the growth and maturation of the ovum a large part of the chromatin of the germinal vesicle may be lost, either by passing out bodily into the cytoplasm, by conversion into supernumerary or accessory nucleoli which finally degenerate, or by being cast out and degenerating at the time the polar bodies are formed (Figs. 97, 128).

---

[1] Häcker ('95, p. 249) has called attention to the fact that the nucleolus is as a rule single in small eggs containing relatively little deutoplasm (cœlenterates, echinoderms, many annelids, and some copepods), while it is multiple in large eggs heavily laden with deutoplasm (lower vertebrates, insects, many crustacea).

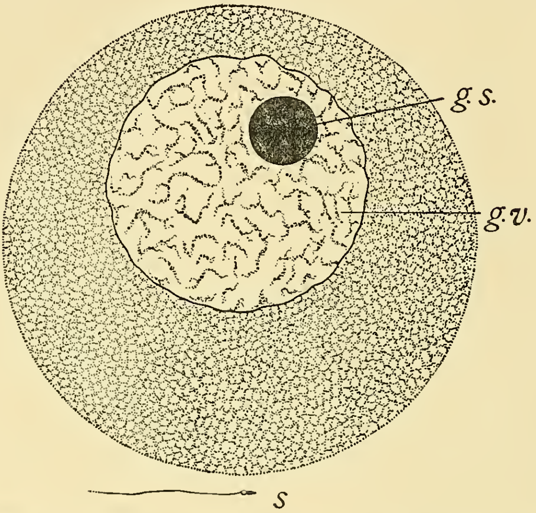

Fig. 58. — Ovarian egg of the sea-urchin, *Toxopneustes* (× 750).

g.v. Nucleus or germinal vesicle, containing an irregular discontinuous network of chromatin; *g.s.* nucleolus or germinal spot, intensely stained with hæmatoxylin. The naked cell-body consists of a very regular alveolar meshwork, scattered through which are numerous minute granules or microsomes. (*Cf.* Figs. 11, 12.) Below, at *s*, is an entire spermatozoön shown at the same enlargement (both middle-piece and flagellum are slightly exaggerated in size).

The nucleolus of the egg-cell is, as elsewhere, a variable quantity and is still imperfectly understood. It often attains an enormous development, forming the "Keimfleck" or "germinal spot" of the early observers. There are some cases (*e.g.* echinoderm eggs) in which it is always a single large spherical body (Fig. 58), and this condition appears to be characteristic of the very young ovarian eggs of most animals. As a rule, however, the number of nucleoli increases with the growth of the ovum, until, in such forms as Amphibia and reptiles, they may be numbered by hundreds.

---

[1] p. 273.

[2] p. 338.

In a large number of cases the nucleoli are of two quite distinct types, which Flemming has distinguished as the "principal nucleolus" (*Hauptnucleolus*) and "accessory nucleoli" (*Nebennucleoli*). These differ widely in staining-reaction; but it does not yet clearly appear whether they definitely correspond to the plasmosomes and karyosomes of tissue-cells (p. 34). The principal nucleolus, which alone is present in such eggs as those of echinoderms, often stains deeply with chromatin-stains, yet differs more or less widely from the chromatin-network,[1] and in some cases at least it does not contribute

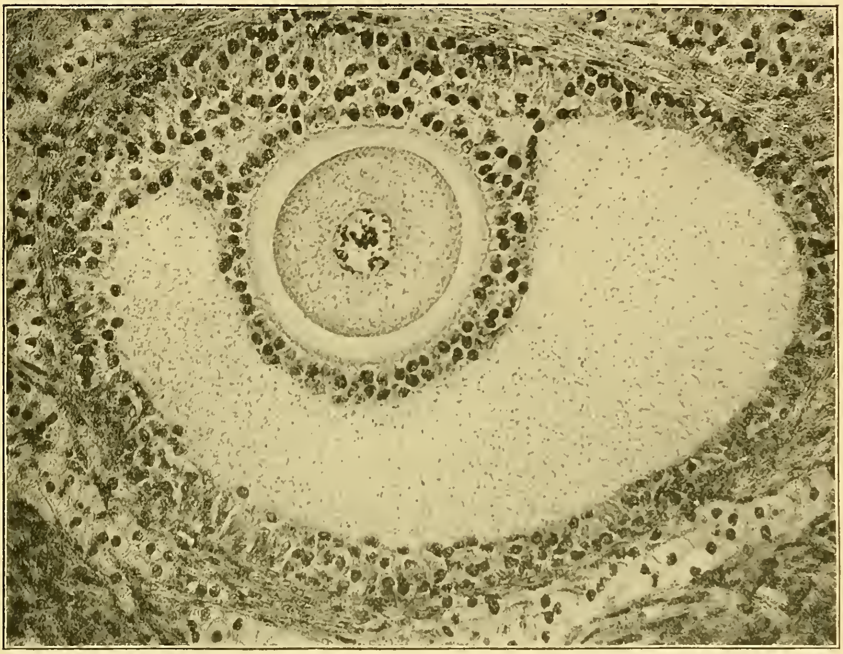

Fig. 59. — Ovum of the cat, within the ovary, directly reproduced from a photograph of a preparation by DAHLGREN. [Enlarged 235 diameters.] The ovum lies in the Graafian follicle within the *discus proligerus*, the latter forming the immediate follicular investment (*corona radiata*) of the egg. Within the *corona* is the clear *zona pellucida* or egg-membrane. (*Cf.* Fig. 92.)

---

[1] *Cf.* List, '96, Montgomery, '98, 2, and Obst., '99.

to the formation of chromosomes. It cannot therefore be directly compared to the net-knots or karyosomes of tissue-cells. This nucleolus is often vacuolated and sometimes assumes the form of a hollow vesicle. It is rarely double or multiple. The accessory nucleoli, on the other hand, are in general coloured by plasma-stains, thus resembling the plasmosomes of tissue-cells; they are often multiple, and as a rule they arise secondarily during the growth of the egg (Fig. 61). The accessory nucleoli often have no connection with the principal; but in some mollusks and annelids an accessory and a principal nucleolus are closely united to form a single compound body (Figs. 60, 61). The numerous nucleoli of the amphibian or reptilian egg appear to be of the "accessory" type. The singular inconstancy of the nucleolus is evidenced by the fact that even closely related species may differ in this regard. Thus, in *Cyclops brevicornis*, according to Häcker, the very young ovum contains a single intensely chromatic nucleolus; at a later period a number of paler accessory nucleoli appear; and still later the principal nucleolus disappears, leaving only the accessory ones. In *C. strenuus*, on the other hand, there is throughout but a single nucleolus.

The physiological meaning of the nucleoli is still involved in doubt. Many cases are, however, certainly known in which the nucleolus plays no part in the later development of the nucleus, being cast out or degenerating *in situ* at the time the polar bodies are formed. It is, for example, cast out bodily in the medusa *Æquorea* (Häcker) and in various annelids and echinoderms, afterward lying for some time as a "metanucleus" in the egg-cytoplasm before degenerating. In these cases the chromosomes are formed in the germinal vesicle independently of the nucleoli (Fig. 125), which degenerate *in situ* when the membrane of the germinal vesicle disappears. In such cases it seems quite certain that the nucleoli do not contribute to the formation of the chromosomes, and that their substance represents passive material which is of no further direct use. Hence we can hardly doubt the conclusion of Häcker, that the nucleoli of the germ-cells are, in some cases at least, accumulations of by-products of the nuclear action, derived from the chromatin either by direct transformation of its substance, or as chemical cleavage-products or secretions. It will be shown in Chapter V. that in some cases a large part of the chromatic reticulum is cast out, and degenerates at the time the polar bodies are formed. The immense growth of the chromatin during the ovarian development is probably correlated in some way with the intense constructive activity of the cytoplasm (p. 339); and when this latter process has ceased a large part of the chromatin-substance, having fulfilled its functions, is cast aside. It seems not improbable that the nucleoli are tributary to the same general process, perhaps

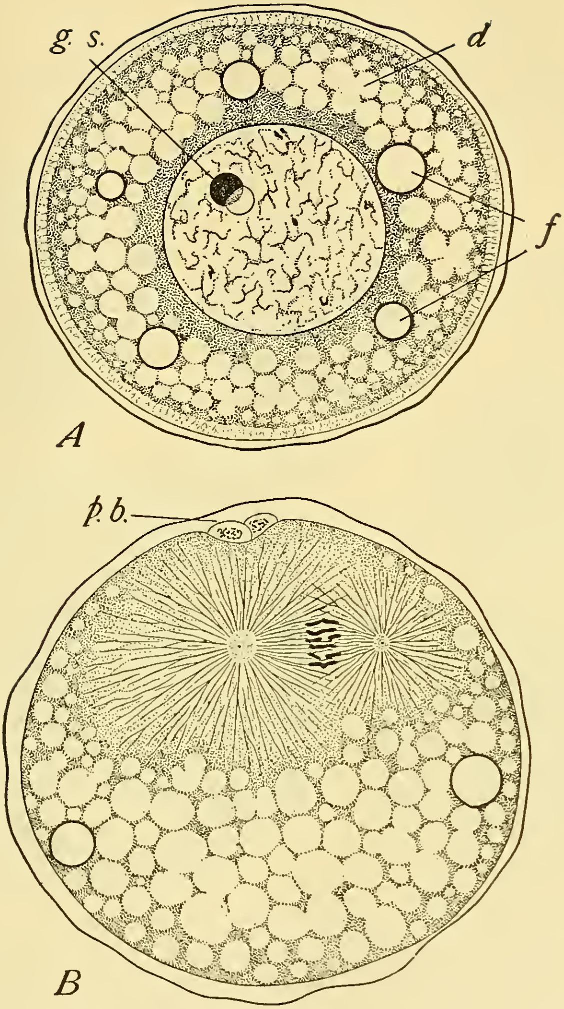

Fig. 60. — Eggs of the annelid *Nereis*, before and after fertilization, × 400 (for intermediate stages see Fig. 95).

A. Before fertilization. The large germinal vesicle occupies a nearly central position. It contains a network of chromatin in which are seen five small darker bodies; these are the quadruple chromosome-groups, or tetrads, in process of formation (not all of them are shown); these alone persist in later stages, the principal mass of the network being lost; *g.s.* double germinal spot, consisting of a chromatic and an achromatic sphere. This egg is heavily laden with yolk, in the form of clear deutoplasm-spheres (*d*) and fat-drops (*f*), uniformly distributed through the cytoplasm. The peripheral layer of cytoplasm (peri-vitelline layer) is free from deutoplasm. Outside this the membrane. *B.* The egg some time after fertilization and about to divide. The deutoplasm is now concentrated in the lower hemisphere, and the peri-vitelline layer has disappeared. Above are the two polar bodies (*p.b.*). Below them lies the mitotic figure, the chromosomes dividing.

serving as storehouses of material formed incidentally to the general nuclear activity, but not of further direct use.

Carnoy and Le Brun ('97, '99) reach, however, the conclusion that in the germinal vesicle of Amphibia the chromosomes are derived not from the chromatin-network, but solely from the nucleoli. The apparent contradiction of this result with that of other observers is, perhaps, only a verbal one; for the "nucleoli" are here evidently chromatin-masses, and the disappearance of the chromatic network is comparable with what occurs at a later period in the annelid egg (Figs. 97, 128).

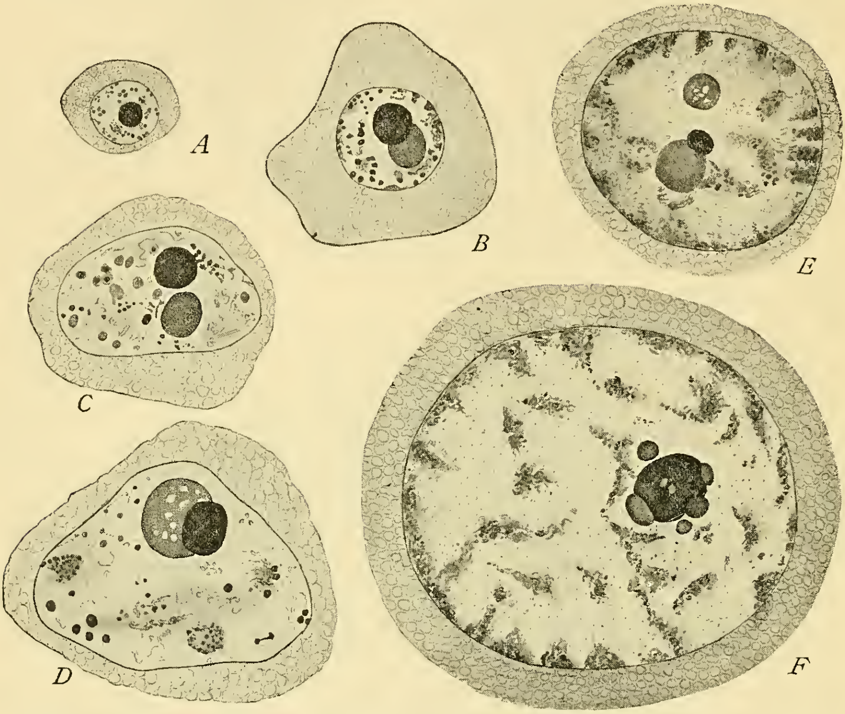

Fig. 61. — Germinal vesicles of growing ovarian eggs of the lamellibranch, *Unio* (*A–D*), and the spider, *Epeira* (*E–F*). [OBST.]

A. Youngest stage with single (principal) nucleolus. *B*. Older egg, showing accessory nucleolus attached to the principal. *C*. The two nucleoli separated. *D*. Much older stage, showing the two nucleoli united. *E*. Germinal vesicle of *Epeira*, showing one accessory nucleolus attached to the principal, and one free. *F*. Later stage; several accessory nucleoli attached to the principal.

2. *The Cytoplasm*

The egg-cytoplasm varies greatly in appearance with the variations of the deutoplasm. In such eggs as those of the echinoderm

(Fig. 58), which have little or no deutoplasm, the cytoplasm forms a regular meshwork, which is in this case an undoubted alveolar structure, the structure of which has already been described at p. 28. In eggs containing yolk the deutoplasm-spheres or granules are laid down in the spaces of the meshwork and appear to correspond to the alveolar spheres of the echinoderm egg (p. 50). If they are of large size the cytoplasm assumes a "pseudo-alveolar" structure (Fig. 60), much as in plant-cells laden with reserve starch; but reasons have already been given (p. 50) for regarding this as only a modification of the "primary" alveolar structure of Bütschli. There is good reason to believe, however, that the egg-cytoplasm may in some cases form a true reticular structure with the yolk-granules lying in its interstices, as many observers have described. In many cases a peripheral layer of the ovum, known as the cortical or peri-vitelline layer, is free from deutoplasm-spheres, though it is continuous with the protoplasmic meshwork in which the latter lie (Fig. 60). Upon fertilization, or sometimes before, this layer may disappear by a peripheral movement of the yolk, as appears to be the case in *Nereis*. In other cases the peri-vitelline substance rapidly flows toward the point at which the spermatozoön enters, where a protoplasmic germinal disc is then formed; for example, in many fish-eggs.

The character of the yolk varies so widely that it can here be considered only in very general terms. The deutoplasm-bodies are commonly spherical, but often show a more or less distinctly rhomboidal or crystalloid form as in Amphibia and some fishes, and in such cases they may sometimes be split up into parallel lamellæ known as *yolk-plates*. Their chemical composition varies widely, judging by the staining-reactions; but we have very little definite knowledge on this subject, and have to rely mainly on the results of analysis of the total yolk, which in the hen's egg is thus shown to consist largely of proteids, nucleo-albumins, and a variety of related substances which are often associated with fatty substances and small quantities of carbohydrates (glucose, etc.). In some cases the deutoplasm-spheres stain intensely with nuclear dyes, such as hæmatoxylin; *e.g.* in many worms and mollusks; in other cases they show a greater affinity for plasma-stains, as in many fishes and Amphibia and annelids (Fig. 60). Often associated with the proper deutoplasm-spheres are drops of oil, either scattered through the yolk (Fig. 60) or united to form a single large drop, as in many pelagic fish-eggs.

The deutoplasm is as a rule heavier than the protoplasm; and in such cases, if the yolk is accumulated in one hemisphere, the egg assumes a constant position with respect to gravity, the egg-axis standing vertically with the animal pole turned upward, as in the frog, the bird, and many other cases. There are, however, many cases in which the egg may lie in any position. When fat-drops are present they usually lie in the vegetative hemisphere, and since they are lighter than the other constituents they usually cause the egg to lie with the animal pole turned downwards, as is the case with some annelids (*Nereis*) and many pelagic fish-eggs.

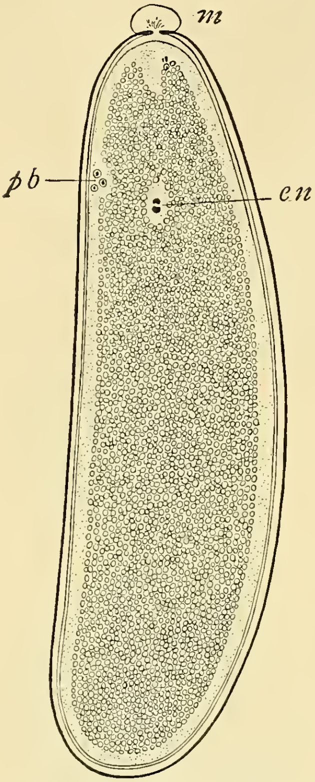

Fig. 62. — Schematic figure of a median longitudinal section of the egg of a fly (*Musca*), showing axes of the bilateral egg and the membranes. [From KORSCHELT and HEIDER, after HENKING and BLOCHMANN.]

e.n. The germ-nuclei uniting; *m.* micropyle; *p.b.* the polar bodies. The flat side of the egg is the dorsal, the convex side the ventral, and the micropyle is at the anterior end. The deutoplasm (small circles) lies in the centre surrounded by a peripheral or peri-vitelline layer of protoplasm. The outer heavy line is the chorion, the inner lighter line the vitelline membrane, both being perforated by the micropyle, from which exudes a mass of jelly-like substance.

3. *The Egg-envelopes*

The egg-envelopes fall under three categories. These are: —

(*a*) The *vitelline membrane*, secreted by the ovum itself.

(*b*) The *chorion*, formed outside the ovum by the activity of the maternal follicle-cells.

(*c*) *Accessory envelopes*, secreted by the walls of the oviduct or other maternal structures after the ovum has left the ovary.

Only the first of these properly belongs to the ovum, the second and third being purely maternal products. There are some eggs, such as those of certain cœlenterates (*e.g. Renilla*), that are naked throughout their whole development. In many others, of which the sea-urchin is a type, the fresh-laid egg is naked but forms a vitelline membrane almost instantaneously after the spermatozoön touches it.[1] In other forms (insects, birds) the vitelline membrane may be present before fertilization, and in such cases the egg is often surrounded by a chorion as well. The latter is usually very thick and firm and may have a shell-like consistency, its surface sometimes showing various peculiar markings, prominences, or sculptured patterns characteristic of the species (insects).[2]

---

[1] That the vitelline membrane does not preëxist seems to be established by the fact that egg-fragments likewise surround themselves with a membrane when fertilized. [HERTWIG.]

[2] In some cases, according to Wheeler, the insect-egg has only a chorion, the vitelline membrane being absent.

The accessory envelopes are too varied to be more than touched upon here. They include not only the products of the oviduct or uterus, such as the albumin, shell-membrane, and shell of birds and reptiles, the gelatinous mass investing amphibian ova, the capsules of molluscan ova and the like, but also nutritive fluids and capsules secreted by the external surface of the body, as in leeches and earthworms.

When the egg is surrounded by a membrane before fertilization it is often perforated by one or more openings known as *micropyles*, through which the spermatozoa make their entrance (Figs. 62, 63). Where there is but one micropyle, it is usually situated very near the upper or anterior pole (fishes, many insects), but it may be at the opposite pole (some insects and mollusks), or even on the side (insects). In many insects there is a group of half a dozen or more micropyles near the upper pole of the egg, and perhaps correlated with this is the fact that several spermatozoa enter the egg, though only one is concerned with the actual process of fertilization.

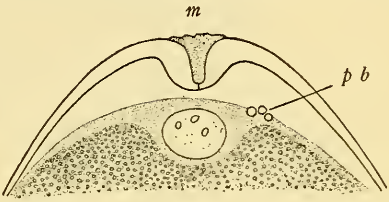

Fig. 63.— Upper pole of the egg of *Argonauta*. [Ussow.]

The egg is surrounded by a very thick membrane, perforated at *m* by the funnel-shaped micropyle; below the latter lies the egg-nucleus in the peri-vitelline layer of protoplasm; *p.b.* the polar bodies.

The plant-ovum, which is usually known as the *oösphere* (Figs. 64, 107), shows the same general features as that of animals, being a relatively large, quiescent, rounded cell containing a large nucleus. It never, however, attains the dimensions or the complexity of structure shown in many animal eggs, since it always remains attached to the maternal structures, by which it is provided with food and invested with protective envelopes. It is therefore naked, as a rule, and is not heavily laden with reserve food-matters such as the deutoplasm of animal ova. A vitelline membrane is, however, often formed soon after fertilization, as in echinoderms. The most interesting feature of the plant-ovum is the fact that it often contains plastids (leucoplasts or chromatophores) which, by their division, give rise to those of the embryonic cells. These sometimes have the form of typical chromatophores containing pyrenoids, as in *Volvox* and many other Algæ (Fig. 64). In the higher forms (archegoniate plants), according to the researches of Schmitz and Schimper, the egg contains numerous minute colourless "leucoplasts," which afterward develop into green chromatophores or into the starch-building amyloplasts. This is a point of great theoretical interest; for the researches of Schmitz, Schimper, and others have rendered it highly probable that these plastids are persistent morphological bodies that arise only by the division of preëxisting bodies of the same kind, and hence may be traced continuously from one generation to another through the germ-cells. In the lower plants (Algæ) they may occur in both germ-cells; in the higher forms they are found in the female alone, and in such cases the plastids of the embryonic body are of purely maternal origin.

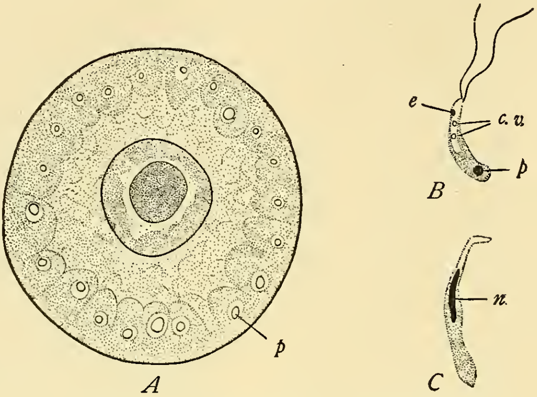

Fig. 64. — Germ-cells of *Volvox*. [OVERTON.]

A. Ovum (oösphere) containing a large central nucleus and a peripheral layer of chromatophores; *p*. pyrenoid. *B*. Spermatozoid; *c.v.* contractile vacuoles; *e*. "eye-spot" (chromoplastid); *p*. pyrenoid. *C*. Spermatozoid stained to show the nucleus (*n*).

B. THE SPERMATOZOÖN

Although spermatozoa were among the first of animal cells observed by the microscope, their real nature was not determined for more than two hundred years after their discovery. Our modern knowledge of the subject may be dated from the year 1841, when Kölliker proved that they were not parasitic animalcules, as the early observers supposed, but the products of cells preëxisting in the parent body. Kölliker, however, did not identify them as cells, but believed them to be of purely nuclear origin. We owe to Schweigger-Seidel and La Valette St. George the proof, simultaneously brought forward by these authors in 1865,[1] that the spermatozoön is a complete cell, consisting of nucleus and cytoplasm, and hence of the same morphological nature as the ovum. It is of extraordinary minuteness, being in many cases less than $\frac{1}{100000}$ the bulk of the ovum.[2]

---

[1] *Arch. Mik. Anat.*, I. '65.

[2] In the sea-urchin, *Toxopneustes*, I estimate its bulk as being between $\frac{1}{400000}$ and $\frac{1}{500000}$ the volume of the ovum. The inequality is in many cases very much greater.

Its precise study is therefore difficult, and it is not surprising that our knowledge of its structure and origin is still far from complete.

1. *Flagellate Spermatozoa*

In its more usual form the animal spermatozoön resembles a minute, elongated tadpole, which swims very actively about by the vibrations of a long, slender tail morphologically comparable with a single cilium or flagellum. Such a spermatozoön consists typically of four parts, as shown in Fig. 65:—

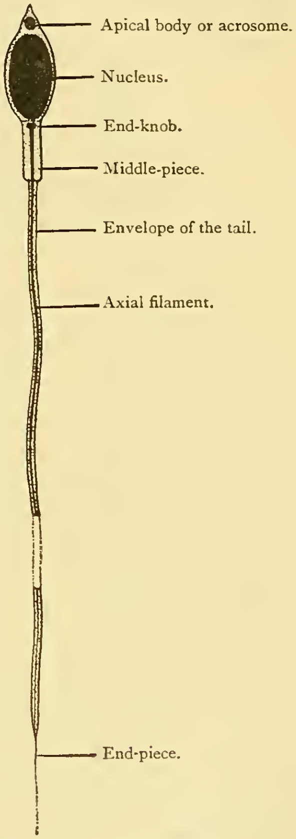

Fig. 65.— Diagram of the flagellate spermatozoön.

1. The *nucleus*, which forms the main portion of the "head," and consists of a very dense and usually homogeneous mass of chromatin staining with great intensity with the so-called "nuclear dyes" (*e.g.* hæmatoxylin or the basic tar-colours such as methyl-green). It is surrounded by a very thin cytoplasmic envelope.

2. An apical body, or *acrosome*, lying at the front end of the head, sometimes very minute, sometimes almost as large as the nucleus, and in some cases terminating in a sharp spur by means of which the spermatozoön bores its way into the ovum.

3. The *middle-piece*, or connecting piece, a larger cytoplasmic body lying behind the head and giving attachment to the tail, from which it is not always distinctly marked off. This body shows the same staining-reactions as the acrosome, having an especial affinity for "plasma-stains" (acid fuchsin, etc.). At its front end it is in some forms (mammals) separated from the nucleus by a short clear region, the *neck*. Like the acrosome, the middle-piece is in some cases derived from an "archoplasmic" mass, representing an attraction-sphere (*Lumbricus*) or a portion of the *Nebenkern* (insects), and it contains, or according to some authors actually arises from, the centrosome (salamander, mammals, insects, etc.).

4. The *tail*, or *flagellum*, in part, at least, a cytoplasmic product developed in connection with the centrosome and "archoplasm"

(attraction-sphere or "Nebenkern") of the mother-cell. It consists of a fibrillated *axial filament* surrounded by a cytoplasmic envelope, and in certain cases (Amphibia) bears on one side a fin-like undulating membrane (Fig. 66). Toward the tip of the flagellum the envelope suddenly disappears or becomes very thin, leaving a short *end-piece* which by some authors is considered to consist of the naked axial filament. The axial filament may be traced through the middle-piece up to the head, at the base of which it usually terminates in a minute body, single or double, known as the *end-knob.* Recent research has proved that the axial filament grows out from the spermatid-centrosome, the latter in some cases persisting as the end-knob (insects, mollusks, mammals), in other cases apparently enlarging to form the main body of the middle-piece (salamander). The tail-envelopes, on the other hand, arise either from the "archoplasm" of the Nebenkern (insects) together with a small amount of unmodified cytoplasm, or from the latter alone (salamander, rat).

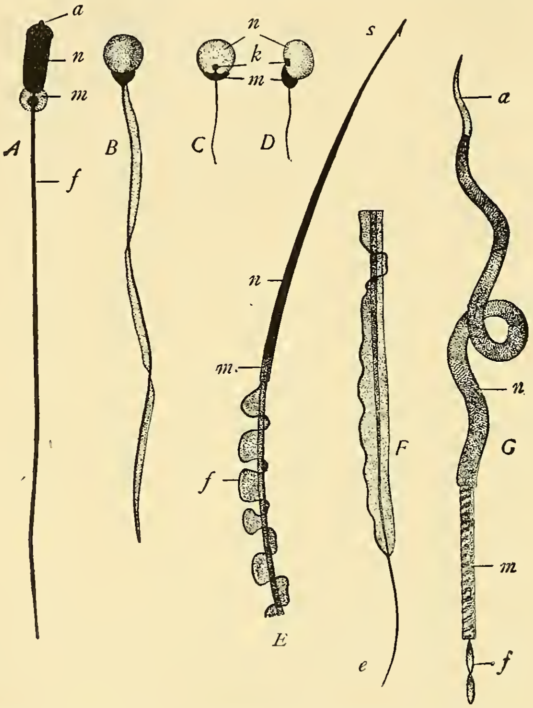

Fig. 66. — Spermatozoa of fishes and Amphibia. [BALLOWITZ.]

A. Sturgeon. *B.* Pike. *C. D. Leuciscus. E. Triton* (anterior part). *F. Triton* (posterior part of flagellum). *G. Raja* (anterior part). *a.* apical body; *e.* end-piece; *f.* flagellum; *k.* end-knob; *m.* middle-piece; *n.* nucleus; *s.* apical spur.

From a physiological point of view we may arrange the parts of the spermatozoön under two categories as follows: —

1. The *essential structures* which play a direct part in fertilization. These are: —
   - (*a*) The *nucleus*, which contains the chromatin.
   - (*b*) The *middle-piece*, which either contains a formed centrosome or pair of centrosomes (end-knob), or is itself a metamorphosed centrosome. This is probably to be regarded as the fertilizing element *par excellence*, since there is reason to believe that when introduced into the egg it gives the stimulus to division.
2. The *accessory structures*, which play no direct part in fertilization, viz.: —
   - (*a*) The *apex* or *spur*, by which the spermatozoön attaches itself to the egg or bores its way into it, and which also serves for the attachment of the spermatozoön to the nurse-cells or supporting cells of the testis.
   - (*b*) The *tail*, a locomotor organ which carries the nucleus and centrosome, and, as it were, deposits them in the egg at the time of fertilization. There can be little doubt that the substance of the flagellum is contractile, and that its movements are of the same nature as those of ordinary cilia. Ballowitz's discovery of its fibrillated structure is therefore of great interest, as indicating its structural as well as physiological similarity to a muscle-fibre. The outgrowth of the axial filament from the centrosome is probably comparable to the formation of spindle-fibres or astral rays, a conclusion of especial interest in its relation to Van Beneden's theory of mitosis (p. 100).

Tailed spermatozoa conforming more or less nearly to the type just described are with few exceptions found throughout the Metazoa from the cœlenterates up to man; but they show a most surprising diversity in form and structure in different groups of animals, and the homologies between the different forms have not yet been fully determined. The simpler forms, for example, those of echinoderms and some of the fishes (Figs. 66 and 100), conform very nearly to the foregoing description. Every part of the spermatozoön may, however, vary more or less widely from it (Figs. 66–68). The head (nucleus) may be spherical, lance-shaped, rod-shaped, spirally twisted, hook-shaped, hood-shaped, or drawn out into a long filament; and it is often divided into an anterior and a posterior piece of different staining-capacity, as is the case with many birds and mammals, but it is probable that the anterior of these may represent the acrosome. An interesting form of head is described by Wheeler ('97) in

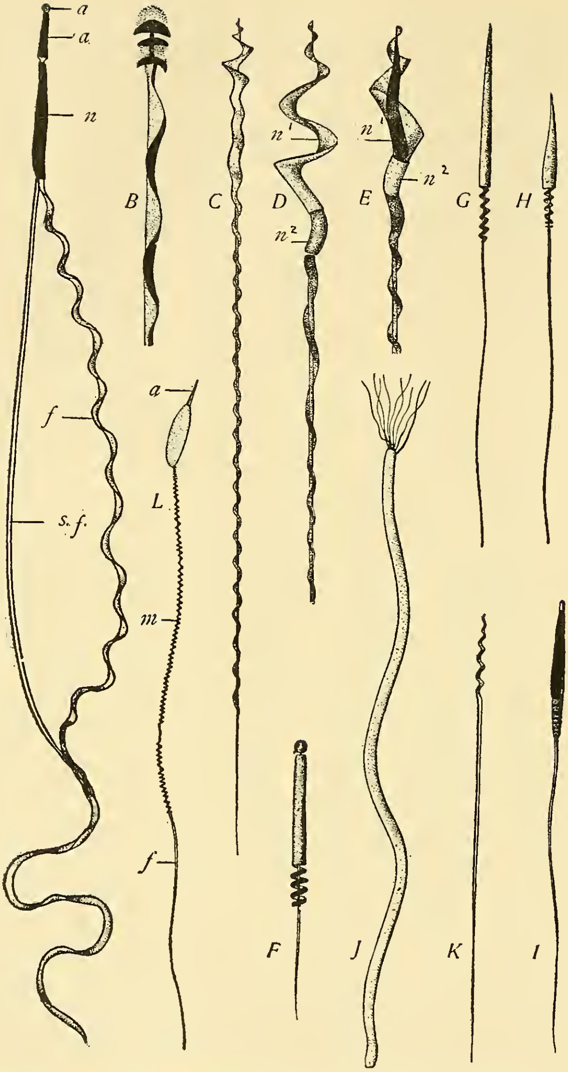

Fig. 67. — Spermatozoa of various animals. [*A–I, L,* from Ballowitz; *J, K,* from von Brunn.]

A (At the left). Beetle (*Copris*), partly macerated to show structure of flagellum; it consists of a supporting fibre (*s.f.*) and a fin-like envelope (*f*); *n.* nucleus; *a. a.* apical body divided into two parts (the posterior of these is perhaps a part of the nucleus). *B.* Insect (*Calathus*), with barbed head and fin-membrane. *C.* Bird (*Phyllopneuste*). *D.* Bird (*Muscicapa*), showing spiral structure; nucleus divided into two parts (n^1, n^2); no distinct middle-piece. *E.* Bulfinch; spiral membrane of head. *F.* Gull (*Larus*) with spiral middle-piece and apical knob. *G. H.* Giant spermatozoön and ordinary form of *Tadorna*. *I.* Ordinary form of the same stained, showing apex, nucleus, middle-piece and flagellum. *J.* "Vermiform spermatozoön" and, *K.* ordinary spermatozoön of the snail *Paludina*. *L.* Snake (*Coluber*), showing apical body (*a*), nucleus, greatly elongated middle-piece (*m*), and flagellum (*f*).

the spermatozoön of *Myzostoma*, where it is a greatly elongated fusiform body, passing insensibly into the tail without distinct middle-piece and containing a single series of chromatin-discs. The number of these in *M. glabrum* is 24, which is the somatic number of chromosomes in this species. In *M. cirriferum* the number of chromatin-discs is more than 60. Somewhat similar spermatozoa occur in the acœlous Turbellaria.[1] The acrosome sometimes appears to be wanting, *e.g.* in some fishes (Fig. 66). When present, it is sometimes a minute rounded knob, sometimes a sharp stylet, and in some cases terminates in a sharp barbed spur by which the spermatozoön appears to penetrate the ovum (*Triton*). In the mammals it is sometimes very small (rat), sometimes very large (guinea-pig), and in some forms is surrounded by a cytoplasmic layer forming the "head-cap" (Figs. 68, 86). It is sometimes divided into two distinct parts, a longer posterior piece and a knob-like anterior piece (insects, according to Ballowitz).

The middle-piece or connecting-piece shows a like diversity (Figs. 66–68). In many cases it is sharply differentiated from the flagellum, being sometimes nearly spherical, sometimes flattened like a cap against the nucleus, and sometimes forming a short cylinder of the same diameter as the nucleus, and hardly distinguishable from the latter until after staining (newt, earthworm). In other cases it is very long (reptiles, some mammals), and is scarcely distinguishable from the flagellum. In still others (birds, some mammals) it passes insensibly into the flagellum, and no sharply marked limit between them can be seen. In many of the mammals the long connecting-piece is separated from the head by a narrow "neck" in which the end-knobs lie, as described below.

Internally, the middle-piece consists of an axial filament and an envelope, both of which are continuous with those of the flagellum. In some cases the envelope shows a distinctly spiral structure, like that of the tail-envelope; but this is not always visible. The most interesting part of the middle-piece is the "end-knob" in which the axial filament terminates, at the base of the nucleus. In some cases this appears to be single. More commonly it consists of two or more minute bodies lying side by side (Fig. 68, *B*, *D*).

The flagellum or tail is merely a locomotor organ which plays no part in fertilization. It is, however, the most complex part of the spermatozoön, and shows a very great diversity in structure. Its most characteristic feature is the *axial filament*, which, as Ballowitz has shown, is composed of a large number of parallel fibrillæ, like a muscle-fibre. This is surrounded by a cytoplasmic envelope, which sometimes shows a striated or spiral structure, and in which, or in connection with which, may be developed secondary or accessory filaments and other structures. At the tip the axial filament may lose its envelope and thus give rise to the so-called "end-piece" (Retzius). In *Triton*, for example (Fig. 66, *F*), the envelope of the axial filament ("principal filament") gives attachment to a remarkable fin-like membrane, having a frilled or undulating free margin along which is developed a "marginal filament." Toward the tip of the tail the fin, and finally the entire envelope, disappears, leaving only the axial filament to form the end-piece. After maceration the envelope shows a conspicuous cross-striation, which perhaps indicates a spiral structure such as occurs in the mammals. The marginal filament, on the other hand, breaks up into numerous parallel fibrillæ, while the axial filament remains unaltered (Ballowitz).

---

[1] *Cf.* Wheeler, p. 7.

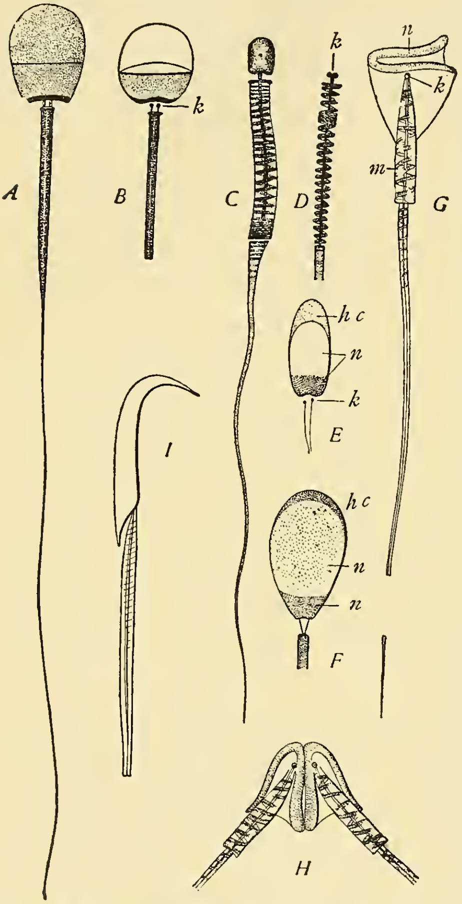

Fig. 68. — Spermatozoa of mammals. [*A–F* from BALLOWITZ.]

A. Badger (living). *B*. The same after staining. *C*. Bat (*Vesperugo*). *D*. The same, flagellum and middle-piece or connecting-piece, showing end-knobs. *E*. Head of the spermatozoön of the bat (*Rhinolophus*) showing details. *F*. Head of spermatozoön of the pig. *G*. Opossum (after staining). *H*. Double spermatozoa from the *vas deferens* of the opossum. *I*. Rat.

h.c. head-cap (acrosome); *k*. end-knob; *m*. middle-piece; *n*. nucleus (in *B*, *E*, *F*, consisting of two different parts).

A fin-membrane has also been observed in some insects and fishes, and has been asserted to occur in mammals (man included). Later observers have, however, failed to find the fin in mammals, and their observations indicate that the axial filament is merely surrounded by an envelope which sometimes shows traces of the same spiral arrangement as that which is so conspicuous in the connecting-piece. In the skate the tail has two filaments, both composed of parallel fibrillæ, connected by a membrane and spirally twisted about each other; a somewhat similar structure occurs in the toad. In some beetles there is a fin-membrane attached to a stiff axial "supporting fibre" (Fig. 67, *A*). The membrane itself is here composed of four parallel fibres, which differ entirely from the supporting fibre in staining-capacity and in the fact that each of them may be further resolved into a large number of more elementary fibrillæ.

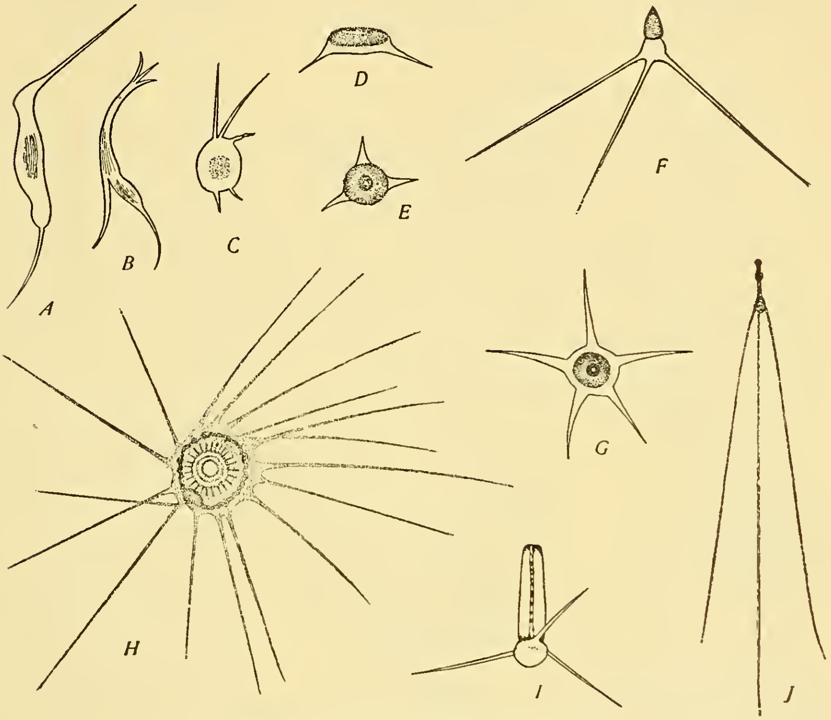

Fig. 69. — Unusual forms of spermatozoa.

A. B. C. Living amœboid spermatozoa of the crustacean *Polyphemus*. [Zacharias.]
D. E. Spermatozoa of crab, *Dromia*. *F.* Of *Ethusa*, *G.* of *Maja*, *H.* of *Inachus*. [Grobben.]
I. Spermatozoön of lobster, *Homarus*. [Herrick.]
J. Spermatozoön of crab, *Porcellana*. [Grobben.]

Many interesting details have necessarily been passed over in the foregoing account. One of these is the occurrence, in some mammals, birds, Amphibia (frog), and mollusks, of two kinds of spermatozoa in the same animal. In the birds and Amphibia the spermatozoa are of two sizes, but of the same form, the larger being known as "giant spermatozoa" (Fig. 67, *G*, *H*). In the gasteropod *Paludina* the two kinds differ entirely in structure, the smaller form being of the usual type and not unlike those of birds, while the larger, or "vermiform," spermatozoa have a worm-like shape and bear a tuft of cilia at one end, somewhat like the spermatozoids of plants (Fig. 67, *J*, *K*). In this case only the smaller spermatozoa are functional (von Brunn).

No less remarkable is the conjugation of spermatozoa in pairs (Fig. 68, *H*), which takes place in the *vas deferens* in the opossum (Selenka) and in some insects (Ballowitz, Auerbach). Ballowitz's researches ('95) on the double spermatozoa of beetles (*Dytiscidæ*) prove that the union is not primary, but is the result of an actual conjugation of previously separate spermatozoa. Not merely two, but three or more spermatozoa may thus unite to form a "spermatozeugma," which swims like a single spermatozoön. Whether the spermatozoa of such a group separate before fertilization is unknown; but Ballowitz has found the groups, after copulation, in the female receptaculum, and he believes that they may enter the egg in this form. The physiological meaning of the process is unknown.

2. *Other Forms of Spermatozoa*

The principal deviations from the flagellate type of spermatozoön occur among the arthropods and nematodes (Fig. 69). In many of these forms the spermatozoa have no flagellum, and in some cases they are actively amœboid; for example, in the daphnid *Polyphemus* (Fig. 69, *A*, *B*, *C*) as described by Leydig and Zacharias. More commonly they are motionless like the ovum. In the chilognathous myriapods the spermatozoön has sometimes the form of a bi-convex lens (*Polydesmus*), sometimes the form of a hat or helmet having a double brim (*Julus*). In the latter case the nucleus is a solid disc at the base of the hat. In many decapod Crustacea the spermatozoön consists of a cylindrical or conical body from one end of which radiate a number of stiff spine-like processes. The nucleus lies near the base. In none of these cases has the centrosome been identified.

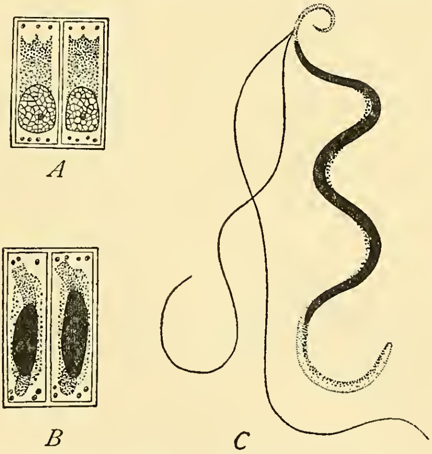

Fig. 70. — Spermatozoids of *Chara*. [BELAJEFF.]

A. Mother-cells with reticular nuclei. *B*. Later stage, with spermatozoids forming. *C*. Mature spermatozoid (the elongate nucleus black).

3. *Paternal Germ-cells of Plants*

In most of the flowering plants the male germ-cells are represented by two "generative nuclei," lying at the tip of the pollen tube (Fig. 106). On the other hand, in the cycads (Figs. 87, 108) and in a large number of the lower plants (pteridophytes, Muscineæ, and many others), the male germ-cell is a minute actively swimming cell, known as the *spermatozoid*, which is closely analogous to the spermatozoön. The spermatozoids are in general less highly differentiated than spermatozoa, and often show a distinct resemblance to the asexual swarmers or zoöspores so common in the lower plants (Figs. 70, 71). They differ in two respects from animal spermatozoa: first in possessing not one but two or several flagella; second, in the fact that these are attached as a rule not to the end of the cell, but on the side. In the lower forms plastids are present in the form of chromatophores, one of which may be differentiated into a red "eye-spot," as in *Volvox* and *Fucus* (Figs. 57, 71, *A*), and they may even contain contractile vacuoles (*Volvox*); but both these structures are wanting in the higher forms. These consist only of a nucleus with a very small amount of cytoplasm, and have typically a spiral form. In *Chara*, where their structure and development have recently been carefully studied by Belajeff, the spermatozoids have an elongated spiral form with two long flagella attached near the pointed end, which is directed forward in swimming (Fig. 70). The main body of the spermatozoid is occupied by a dense, apparently homogeneous nucleus surrounded by a very delicate layer of cytoplasm. Behind the nucleus lies a granular mass of cytoplasm, forming one end of the cell, while in front is a slender cytoplasmic tip to which the flagella are attached. Nearly similar spermatozoids occur in the liverworts and mosses. In the ferns and other pteridophytes a somewhat different type occurs

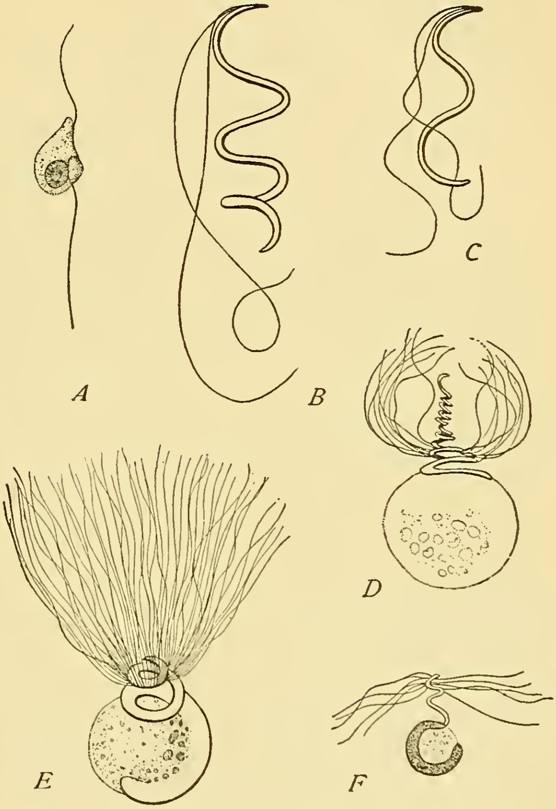

Fig. 71. — Spermatozoids of plants. [*A*, *B*, *C*, *E*, after GUIGNARD; *D*, *F*, after STRASBURGER.]

A. Of an alga (*Fucus*); a red chromatophore at the right of the nucleus. *B*. Liverwort (*Pellia*). *C*. Moss (*Sphagnum*). *D*. *Marsilia*. *E*. Fern, (*Angiopteris*). *F*. Fern, *Phegopteris* (the nucleus dark). (*Cf.* Figs. 87, 88.)

(Figs. 71, 88). Here the spermatozoid is twisted into a conical spiral and bears numerous cilia attached along the upper turns of the spire. The nucleus occupies the lower turns, and attached to them is a large spheroidal cytoplasmic mass, which is cast off when the spermatozoid is set free or at the time it enters the archegonium. This, according to Strasburger, probably corresponds to the basal cytoplasmic mass of *Chara*. The upper portion of the spire to which the cilia are attached is composed of cytoplasm alone, as in *Chara*. Ciliated spermatozoids, nearly similar in type to those of the higher cryptogams, have recently been discovered in the cycads by Hirase (*Gingko*), Ikeno (*Cycas*), and Webber (*Zamia*). They are here hemispherical or pear-shaped bodies of relatively huge size (in Zamia upward of 250 μ in length), with a large nucleus filling most of the cell and a spiral band of cilia making from two to six turns about the smaller end (Figs. 87, 108).

As will be shown farther on (p. 173), the "anterior" cytoplasmic region of the spermatozoid, to which the cilia are attached, is probably the analogue of the middle-piece of the animal spermatozoön; and the work of Belajeff, Strasburger, Ikeno, Hirase, Webber, and Shaw gives good ground for the conclusion that it has an essentially similar mode of origin, though we are still unable to say exactly how far the comparison can be carried. The "posterior" region of the spermatozoid appears to correspond, broadly speaking, to the acrosome.

C. Origin of the Germ-cells

Both ova and spermatozoa take their origin from cells known as primordial germ-cells, which become clearly distinguishable from the somatic cells at an early period of development, and are at first exactly alike in the two sexes. What determines their subsequent sexual differentiation is unknown save in a few special cases. From such data as we possess, there is very strong reason to believe that, with a few exceptions, the primordial germ-cells are sexually indifferent, *i.e.* neither male nor female, and that their transformation into ova or spermatozoa is not due to an inherent predisposition, but is a reaction to external stimulus. Most of the observations thus far made indicate that this stimulus is given by the character of the food, and that the determination of sex is therefore in the last analysis a problem of nutrition. Thus Mrs. Treat ('73) found that if caterpillars were starved before entering the chrysalis state they gave rise to a preponderance of male imagoes, while conversely those of the same brood that were highly fed produced an excess of females. Yung ('81) reached the same result in the case of Amphibia, highly fed tadpoles producing a great excess of females (in some cases as high as 92%) and underfed ones an excess of males. The same result, again, is given by the interesting experiments of Nussbaum ('97) on the rotifer *Hydatina*, which is an especially favourable case since sex is here determined at a very early period, *before the egg is laid*, the eggs being of two sizes, of which the smaller give rise only to males, and the larger only to females. The earlier experiments of Maupas ('91) on this form seemed to show conclusively that the decisive factor was temperature acting on the parent organism, since in a high temperature an excess of females produced male eggs, and in a low temperature the reverse result ensued. Nussbaum shows, however, that this is not a direct effect of temperature, but an indirect one due to the greater birth-rate and the greater activity of the animals under a higher temperature, which result in a speedier exhaustion of food. Direct experiment shows that, under equal temperature-conditions, well-fed females produce a preponderance of female offspring, and *vice versa*, precisely as in the Lepidoptera and Amphibia. These cases show that sex may be determined by conditions of nutrition either affecting the embryo itself (Lepidoptera, Amphibia) long after the egg is laid, or by similar conditions affecting the parent-organism and through it the ovarian egg.

Nutrition is, however, not the only determining cause of sex, as is shown by the long-known case of the honey-bee. Here sex is determined by fertilization, the males arising only from unfertilized eggs by parthenogenesis, while the fertilized eggs give rise exclusively to females, which develop into fertile forms (queens) or sterile forms (workers), according to the nature of the food. This is a very exceptional case, yet here too it is the more highly fed larvæ that produce fertile females. It is interesting to compare with this case that of the plant-lice or aphides. In these forms the summer broods, living under favourable conditions of nutrition, produce only females the eggs of which develop parthenogenetically. In the autumn, under less favourable conditions, males as well as females are produced; and that this is due to the external conditions and not to a fixed cyclical change of the organism is proved by the fact that in the favourable environment of a greenhouse the production of females alone may continue for years.[1]

We are not yet able to state whether there is any one causal element common to all known cases of sex-determination. The observations cited above, as well as a multitude of others that cannot here be reviewed, render it certain, however, that sex as such is not inherited. What is inherited is the capacity to develop into either male or female, the actual result being determined by the combined effect of conditions external to the primordial germ-cell.

---

[1] See Geddes, *Sex*, in *Encyclopædia Britannica;* Geddes and Thompson, *The Evolution of Sex*, 1889; Brooks, *The Law of Heredity*, 1883; Watasé ('92), *The Phenomena of Sex-differentiation*.

In the greater number of cases the primordial germ-cells arise in a germinal epithelium which, in the cœlenterates (Fig. 72), may be a part of either the ectoderm or entoderm, and, in the higher types, is a modified region of the peritoneal epithelium lining the body-cavity. In such cases the primordial germ-cells may be scarcely distinguishable at first from the somatic cells of the epithelium. But in other cases the germ-cells may be traced much farther back in the development, and they or their progenitors may sometimes be identified in the gastrula or blastula stage, or even in the early cleavage-stages. Thus in the worm *Sagitta*, Hertwig has traced the germ-cells back to two primordial germ-cells lying at the apex of the archenteron. In some of the insects they appear still earlier as the products of a large "pole-cell" lying at one end of the segmenting ovum, which divides into two and finally gives rise to two symmetrical groups of germ-cells. Häcker has recently traced very carefully the origin of the primordial germ-cells in *Cyclops* from a "stem-cell" (Fig. 74) clearly distinguishable from surrounding cells in the early blastula stage, not only by its size, but also by its large nuclei rich in chromatin, and by its peculiar mode of mitosis, as described beyond.

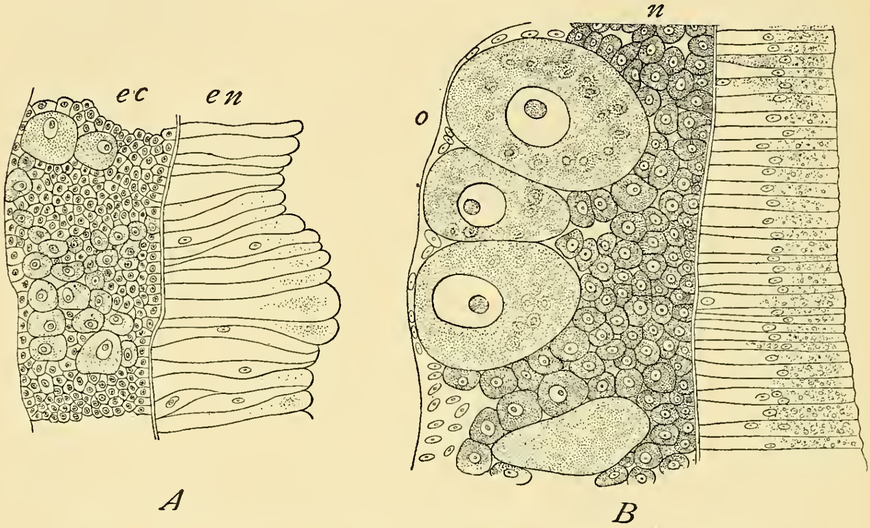

Fig. 72. — Origin of the germ-cells in a hydro-medusa, *Cladonema*. [WEISMANN.]

A. Young stage; section through wall of manubrium of the medusa; ova developing in the ectoderm (*ec*). *B*. Later stage, showing older ova (*o*) and "nutritive cells" (*n*). The ova contain small nuclei probably derived from engulfed nutritive cells.

The most beautiful and remarkable known case of early differentiation of the germ-cells is that of *Ascaris*, where Boveri was able to trace them back continuously through all the cleavage-stages to the two-cell stage! Moreover, from the outset the progenitor of the germ-cells *differs from the somatic cells not only in the greater size and richness of chromatin of its nuclei, but also in its mode of mitosis;* for in all those blastomeres destined to produce somatic cells a portion of

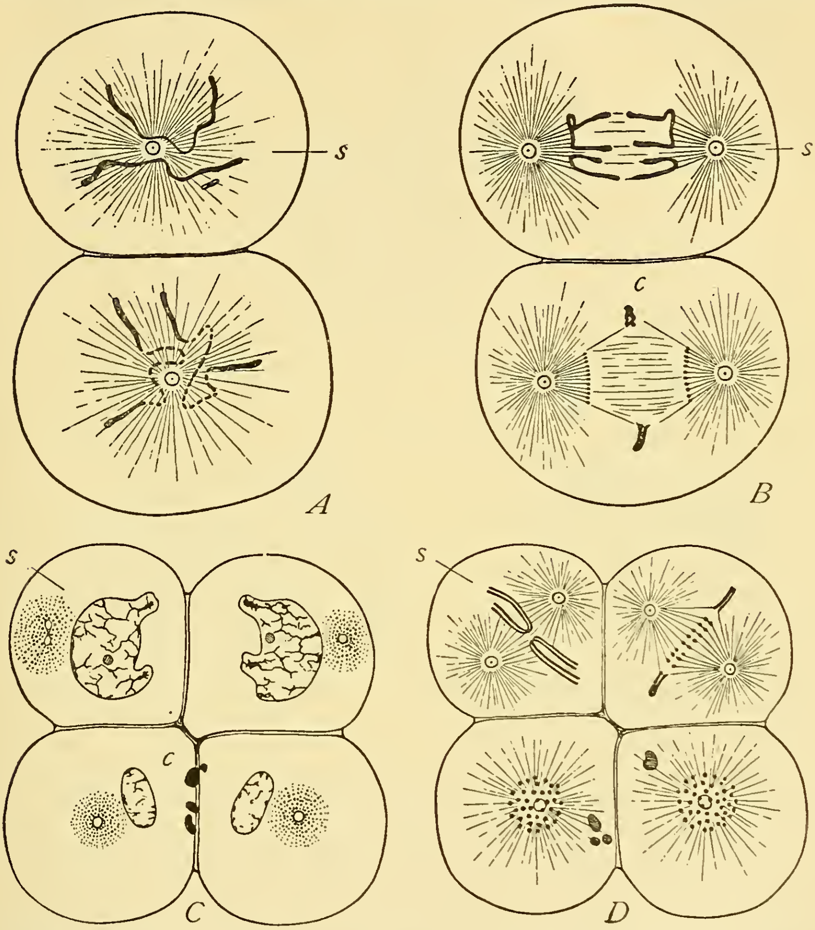

Fig. 73. — Origin of the primordial germ-cells and casting out of chromatin in the somatic cells of *Ascaris*. [Boveri.]

A. Two-cell stage dividing; *s*. stem-cell, from which arise the germ-cells. *B*. The same from the side, later in the second cleavage, showing the two types of mitosis and the casting out of chromatin (*c*) in the somatic cell. *C*. Resulting 4-cell stage; the eliminated chromatin at *c*. *D*. The third cleavage, repeating the foregoing process in the two upper cells.

the chromatin is cast out into the cytoplasm, where it degenerates, and *only in the germ-cells is the sum-total of the chromatin retained.* In *Ascaris megalocephala univalens* the process is as follows (Fig. 73): Each of the first two cells receives two elongated chromosomes. As the ovum prepares for the second cleavage, the two chromosomes reappear in each, but differ in their behaviour (Fig. 73, *A*, *B*). In one of them, which is destined to produce only somatic cells, the thickened ends of each chromosome are cast off into the cytoplasm and degenerate. Only the thinner central part is retained and distributed to the daughter-cells, breaking up meanwhile into a large number of segments which split lengthwise in the usual manner. In the other cell, which may be called the *stem-cell* (Fig. 73, *s*), all the chromatin is preserved and the chromosomes do not segment into smaller pieces. The results are plainly apparent in the four-cell stage, the two somatic nuclei, which contain the reduced amount of chromatin, being small and pale, while those of the two stem-cells are far larger and richer in chromatin (Fig. 73, *C*). At the ensuing division (Fig. 73, *D*) the numerous minute segments reappear in the two somatic cells, divide, and are distributed like ordinary chromosomes; and the same is true of all their descendants thenceforward. The other two cells (containing the large nuclei) exactly repeat the history of the two-cell stage, the two long chromosomes reappearing in each of them, becoming segmented and casting off their ends in one, but remaining intact in the other, which gives rise to two cells with large nuclei as before. This process is repeated five times (Boveri) or six (Zur Strassen), after which the chromatin-elimination ceases, and the two stem-cells or primordial germ-cells thenceforward give rise only to other germ-cells and the entire chromatin is preserved. Through this remarkable process it comes to pass that in this animal *only the germ-cells receive the sum-total of the egg-chromatin handed down from the parent. All of the somatic cells contain only a portion of the original germ-substance.* "The original nuclear constitution of the fertilized egg is transmitted, as if by a law of primogeniture, only to one daughter-cell, and by this again to one, and so on; while in the other daughter-cells the chromatin in part degenerates, in part is transformed, so that all of the descendants of these side-branches receive small reduced nuclei."[1]

It would be difficult to overestimate the importance of this discovery; for although it stands at present an almost isolated case, yet it gives us, as I believe, the key to a true theory of differentiation development,[2] and may in the end prove the means of explaining many phenomena that are now among the unsolved riddles of the cell.

Häcker ('95) has shown that the nuclear changes in the stem-cells and primordial eggs of *Cyclops* show some analogy to those of *Ascaris*, though no casting out of chromatin occurs. The nuclei are very large and rich in chromatin as compared with the somatic cells, and the number of chromosomes, though not precisely determined,

---

[1] Boveri, '91, p. 437.

[2] *Cf.* p. 426.

is less than in the somatic cells (Fig. 74). Vom Rath, working in the same direction, believes that in the salamander also the number of chromosomes in the early progenitors of the germ-cells is one-half that characteristic of the somatic cells.[1] In both these cases, the chromosomes are doubtless bivalent, representing two chromosomes joined together. In *Ascaris*, in like manner, each of the two chromosomes of the stem-cell or primordial germ-cells is probably plurivalent, and represents a combination of several units of a lower order which separate during the segmentation of the thread when the somatic mitosis occurs.

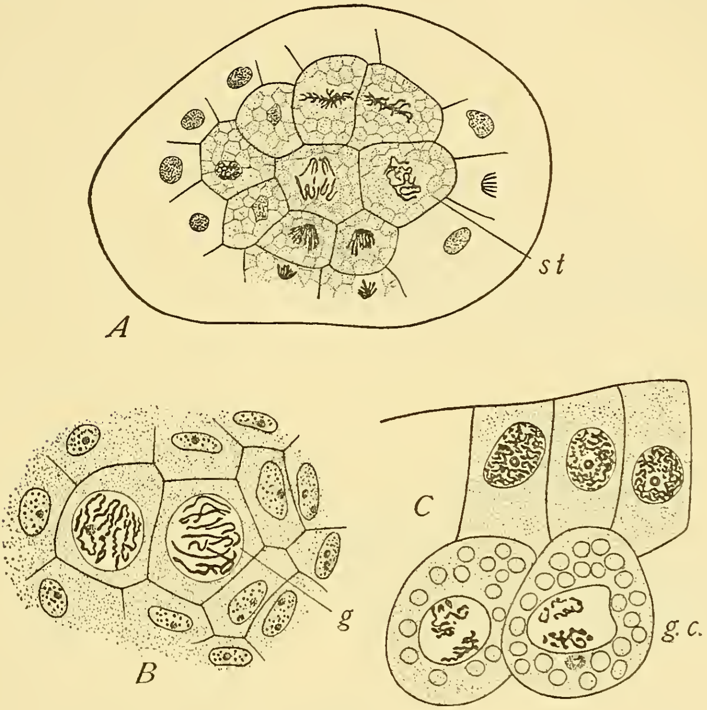

Fig. 74. — Primordial germ-cells in *Cyclops*. [HÄCKER.]

A. Young embryo, showing stem-cell (*st*). *B*. The stem-cell has divided into two, giving rise to the primordial germ-cell (*g*). *C*. Later stage, in section; the primordial germ-cell has migrated into the interior and divided into two; two groups of chromosomes in each.

---

[1] *Cf.* p. 256, Chapter V.

D. GROWTH AND DIFFERENTIATION OF THE GERM-CELLS

I. *The Ovum*

(*a*) *Growth and Nutrition.* — Aside from the transformations of the nucleus, which are considered elsewhere, the story of the ovarian history of the egg is largely a record of the changes involved in nutrition and the storage of material. As the primordial germ-cells enlarge to form the mother-cells of the eggs, they almost invariably become intimately associated with neighbouring cells which not only support and protect them, but also serve as a means for the elaboration of food for the growing egg-cell. One of the simplest arrangements is that occurring in cœlenterates, where the egg lies loose either in one of the general layers or in a mass of germinal tissue, and may crawl actively about among the surrounding cells like an *Amœba*. In such cases (hydroids) the egg may actually feed upon the surrounding cells, taking them bodily into its substance or fusing with them[1] and assimilating their substance with its own. In such cases (*Tubularia*, *Hydra*) the nuclei of the food-cells long persist in the egg-cytoplasm, forming the so-called "pseudo-cells," but finally degenerate and are absorbed by the egg. It would here seem as if a struggle for existence took place among the young ovarian cells, the victorious individuals persisting as the eggs; and this view is probably applicable also to the more usual case where the egg is only indirectly nourished by its brethren.

In most cases, as ovarian development proceeds, a definite association is established between the egg and the surrounding cells. In one of the most frequent arrangements the ovarian cells form a regular layer or *follicle* about the ovum (Figs. 59, 79), and there is very strong reason to believe that the follicle-cells are immediately concerned with the conveyance of nutriment to the ovum. A number of observers have maintained that the follicle-cells may actually migrate into the interior of the egg, and this seems to be definitely established in the case of the tunicates and mollusks (Fig. 75).[2] Such cases are, however, extremely rare; and, as a rule, the material elaborated by the nutritive cells is passed into the egg either in solution or in the form of granular or protoplasmic substance.[3] An interesting case of this kind occurs in the cycads, where, according to Ikeno ('98), the egg-cell is connected with the surrounding cells by broad protoplasmic bridges through which cytoplasmic material flows directly into the egg-cell.

Very curious and suggestive conditions occur among the annelids and insects. In the annelids the nutritive cells often do not form a follicle, but in some forms each egg is accompanied by a single nurse-cell, attached to its side, with which it floats free in the body-cavity. In *Ophryotrocha*, where it has been carefully described by Korschelt, the nurse-cell is at first much larger than the egg itself, and contains a large, irregular nucleus, rich in chromatin (Fig. 76). The egg-cell rapidly grows, apparently at the expense of the nurse-cell, which becomes reduced to a mere rudiment attached to one side of the egg and finally disappears. There can hardly be a doubt, as Korschelt maintains, that the nurse-cell is in some manner connected with the elaboration of food for the growing egg-cell; and the intensely chromatic character of the nucleus is well worthy of note in this connection. Still more interesting are the conditions observed by Wheeler ('96, '97) in *Myzostoma*, where the young egg is accompanied by two nurse-cells, one at either end. These cells fuse bodily with the egg, one having "something to do in forming the vacuolated cytoplasm at the animal pole, . . . the other in forming the granular cytoplasm at the vegetative pole" ('97, p. 42). The polar axis thus determined persists as that of the ripe ovum. This seems one of the clearest cases showing the establishment of the egg-polarity through the relation of the egg to its environment.[1]

---

[1] *Cf.* Doflein, '97.

[2] See Floderus, '95, and Obst, '99.

[3] *Cf.* p. 349.

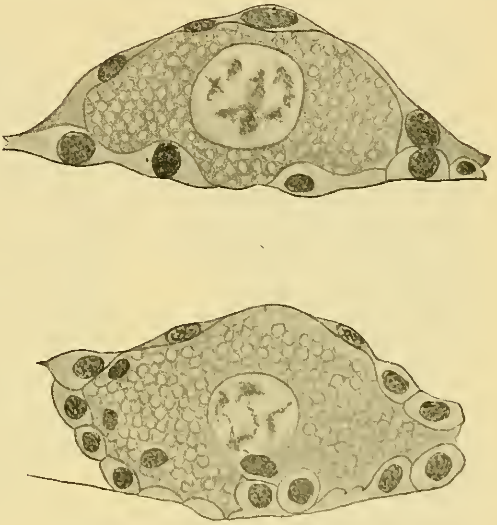

Fig. 75. — Ovarian eggs of *Helix*. [OBST.]

A. Earlier stage, surrounded by follicle. *B*. Later stage, showing inward migration and absorption of follicle-cells.

Somewhat similar nurse-cells occur in the insects, where they have been carefully described by Korschelt. The eggs here lie in a series in the ovarian "egg-tubes" alternating with nutritive cells variously arranged in different cases. In the butterfly *Vanessa*, each egg is surrounded by a regular follicular layer of cells, a few of which at one end are differentiated into nurse-cells. These cells are very large and have huge amœboid nuclei, rich in chromatin (Fig. 77, *A*). In the ear-wig, *Forficula*, the arrangement is still more remarkable, and recalls that occurring in *Ophryotrocha*. Here each egg lies in the egg-tube just below a very large nurse-cell, which, when fully developed, has an enormous branching nucleus as shown in Fig. 163. In these two cases, again, the nurse-cell is characterized by the extraordinary development of its nucleus — a fact which points to an intimate relation between the nucleus and the metabolic activity of the cell.[1]

---

[1] *Cf.* p. 386.

In all these cases it is doubtful whether the nurse-cells are sister-cells of the egg which have sacrificed their own development for the sake of their companions, or whether they have had a distinct origin from a very early period. That the former alternative is possible is shown by the fact that such a sacrifice occurs in some animals after the eggs have been laid. Thus in the earthworm, *Lumbricus terrestris*, several eggs are laid, but only one develops into an embryo, and the latter devours the undeveloped eggs. A similar process occurs in the marine gasteropods, where the eggs thus sacrificed may undergo certain stages of development before their dissolution.[2]

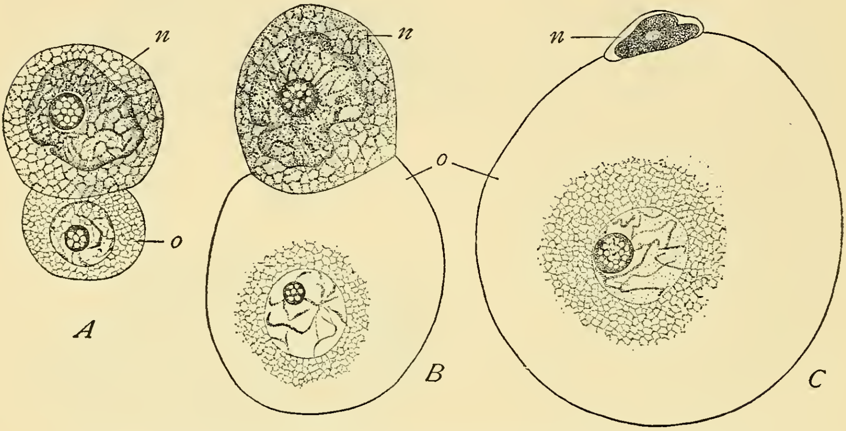

Fig. 76. — Egg and nurse-cell in the annelid, *Ophryotrocha*. [Korschelt.]

A. Young stage, the nurse-cell (*n*) larger than the egg (*o*). *B*. Growth of the ovum. *C*. Late stage, the nurse-cell degenerating.

(*b*) *Differentiation of the Cytoplasm and Deposit of Deutoplasm.* — In the very young ovum the cytoplasm is small in amount and free from deutoplasm. As the egg enlarges, the cytoplasm increases enormously, a process which involves both the growth of the protoplasm and the formation of passive deutoplasm-bodies suspended in the protoplasmic network. During the growth-period a peculiar body known as the *yolk-nucleus* appears in the cytoplasm of many ova, and this is probably concerned in some manner with the growth of the cytoplasm and the formation of the yolk. Both its origin and its physiological *rôle* are, however, still involved in doubt.

---

[1] See p. 338.

[2] See McMurrich, '96.

The deutoplasm first appears, while the eggs are still very small, in the form of granules which seem to have at first no constant position with reference to the egg-nucleus, even in the same species. Thus Jordan ('93) states that in the newt (*Diemyctylus*) the yolk may be first formed at one side of the egg and afterward spread to other parts, or it may appear in more or less irregular separate patches which finally form an irregular ring about the nucleus, which at this period has an approximately central position. In some Amphibia the deutoplasm appears near the periphery and advances inward toward the nucleus. More commonly it first appears in a zone surrounding the nucleus (Fig. 78, *C*, *D*) and advances thence toward the periphery (trout, Henneguy; cephalopods, Ussow). In still others (*e.g.* in myriapods, Balbiani) it appears in irregular patches scattered quite irregularly through the ovum (Fig. 78, *A*). In *Branchipus* the yolk is laid down at the centre of the egg, while the nucleus lies at the extreme periphery (Brauer). These variations show in general no definite relation to the ultimate arrangement — a fact which proves that the eccentricity of the nucleus and the polarity of the

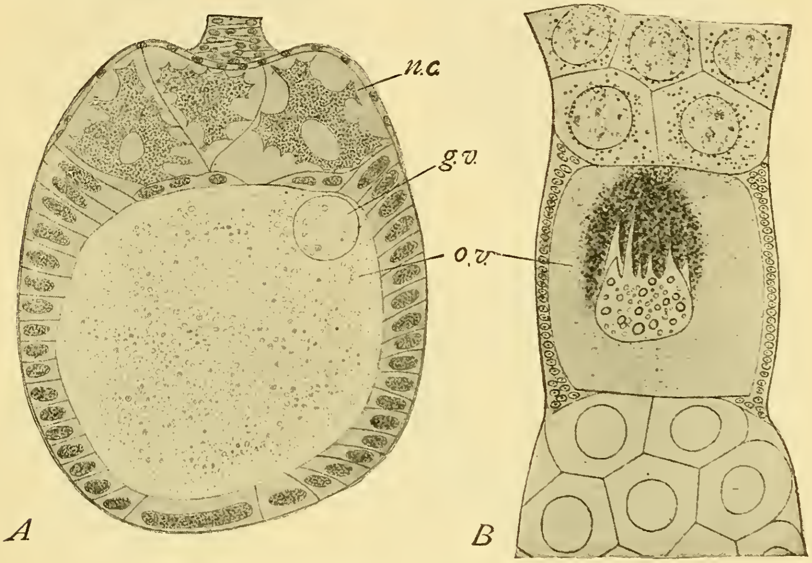

Fig. 77. — Ovarian eggs of insects. [KORSCHELT.]

A. Egg of the butterfly, *Vanessa*, surrounded by its follicle; above, three nurse-cells (*n.c.*) with branching nuclei; *g.v.* germinal vesicle. *B*. Egg of water-beetle, *Dytiscus*, living; the egg (*o.v.*) lies between two groups of nutritive cells; the germinal vesicle sends amœboid processes into the dark mass of food-granules.

egg cannot be explained as the result of a simple mechanical displacement of the germinal vesicle by the yolk, as some authors have maintained.

The primary origin of the deutoplasm-grains is a question that involves the whole theory of cell-action and the relation of nucleus and cytoplasm in metabolism. The evidence seems perfectly clear that in many cases the deutoplasm arises *in situ* in the cytoplasm like the zymogen-granules in gland-cells. But there is now also a very considerable body of evidence indicating that a part of the egg-cytoplasm is directly or indirectly derived from the nucleus through the agency of the yolk-nucleus or otherwise; and the

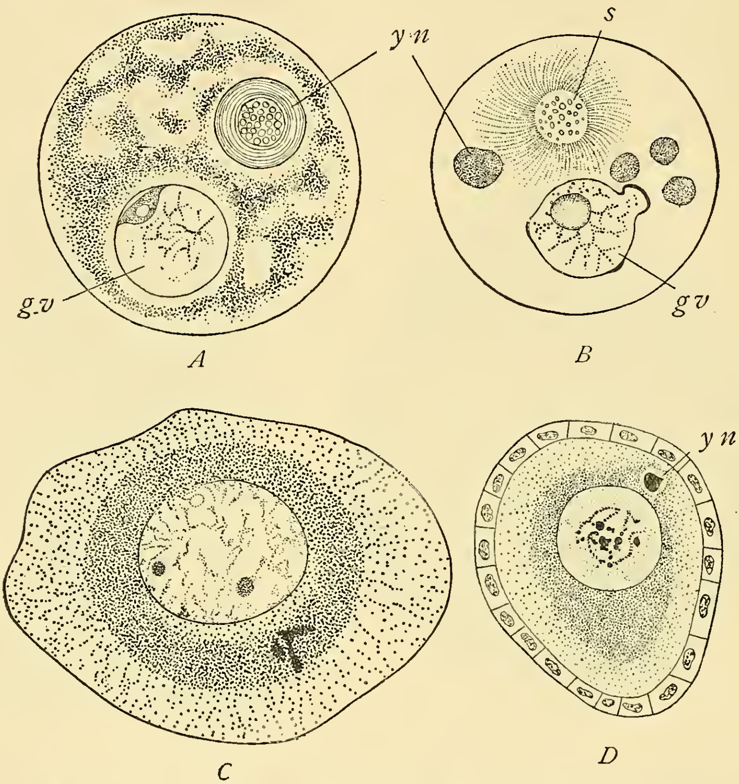

Fig. 78. — Young ovarian eggs, showing yolk-nuclei and deposit of deutoplasm.

A. Myriapod (*Geophilus*) with single "yolk-nucleus" (perhaps an attraction-sphere) and scattered deutoplasm. [BALBIANI.]

B. The same with several yolk-nuclei, and "attraction-sphere," *s*. [BALBIANI.]

C. Fish (*Scorpæna*), with deutoplasm forming a ring about the nucleus, and an irregular mass of "eliminated chromatin" (? yolk-nucleus). [VAN BAMBEKE.]

D. Ovarian egg of young duck (three months) surrounded by a follicle, and containing a "yolk-nucleus," *y.n.* [MERTENS.]

subject can best be considered after an account of that body. It may be mentioned here, however, that a large number of observers have maintained a giving off of nuclear substance to the cytoplasm, in the form of actual buds from the nucleus (Blochmann, Scharff, Balbiani, etc.) as separate chromatin-rods or portions of the chromatin network (Fol, Blochmann, Van Bambeke, Erlanger, Mertens, Calkins, Nemec, etc.) or as nucleolar substance (Leydig, Balbiani, Will, Leydig, Henneguy), but nearly all of these cases demand reëxamination.

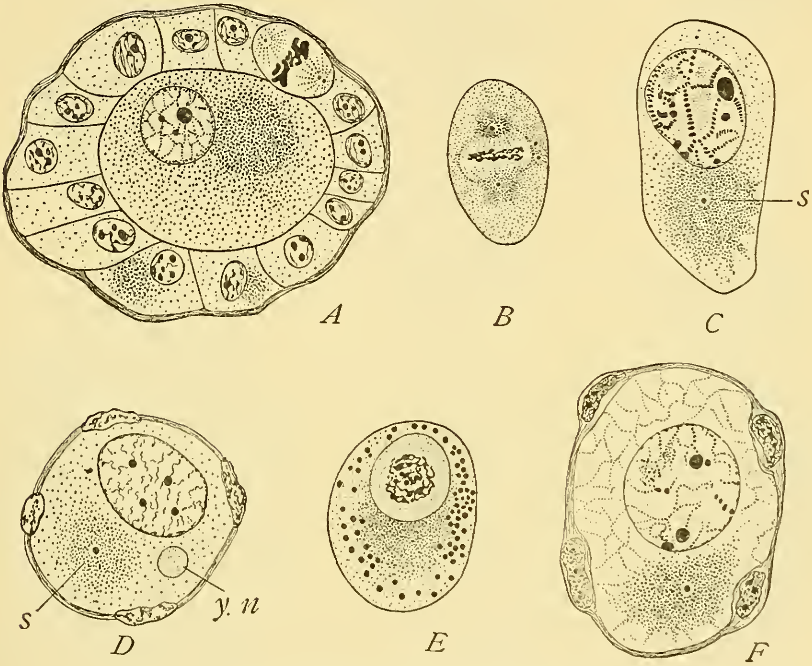

Fig. 79.— Young ovarian eggs of birds and mammals. [Mertens.]

A. Egg of young magpie (eight days), surrounded by the follicle and containing germinal vesicle and "attraction-sphere." *B.* Primordial egg (oögonium) of new-born cat, dividing. *C.* Egg of new-born cat containing "attraction-sphere" (*s*) and centrosome. *D.* Of young thrush surrounded by follicle and containing besides the nucleus an attraction-sphere and centrosome (*s*), and a yolk-nucleus (*y.n.*). *E.* Of young chick containing nucleus, attraction-sphere, and fatty deutoplasm-spheres (black). *F.* Egg of new-born child, surrounded by follicle and containing nucleus and attraction-sphere.

(*c*) *Yolk-nucleus.*—The term *yolk-nucleus* or vitelline body (*Dotterkern, corps vitellin*) has been applied to various bodies or masses that appear in the cytoplasm of the growing ovarian egg; and it must be said that the word has at present no well-defined meaning. As originally described by von Wittich ('45) in the eggs of spiders, and later by Balbiani ('93) in those of certain myriapods, the yolk-nucleus has the form of a single well-defined spheroidal mass which appears at a very early period and persists throughout the later ovarian history. In other forms there are several so-called "yolk-nuclei," sometimes of fairly definite form as described in the Amphibia by Jordan ('93) and in some of the myriapods by Balbiani ('93). In some forms the numerous "yolk-nuclei" are irregular, ill-defined granular masses scattered through the cytoplasm, as described by Stuhlman ('86) in the eggs of insects. In still others the "yolk-nucleus" or "vitelline body" closely simulates an attraction-sphere, being surrounded by distinct astral radiations and enclosing one or more central granules like centrosomes (*Geophilus*, Balbiani, '93, and *Limulus*, Munson, '98). Balbiani is thus led to regard the yolk-nucleus in general as being a metamorphosed attraction-sphere. Miss Foot ('96) has brought forward evidence to show that the polar rings, observed in the eggs of certain leeches and earthworms, are also to be regarded as "yolk-nuclei" (Fig. 102). Henneguy ('93, '96) finally compares the yolk-nucleus to the macronucleus of the Infusoria (!).

In the present state of the subject it is quite impossible to reconcile the discordant accounts that have been given regarding the structure, origin, and fate of the "yolk-nuclei", and from the facts thus far determined we can only conclude that the various forms of "yolk-nuclei" have little more in common than the name. It is, in the first place, doubtful whether the "yolk-nuclei" simulating an attraction-sphere have anything in common with the other forms; and Mertens ('93), Munson ('98), have shown that the young ovarian ova of various birds and mammals (including man) and of *Limulus* contain one or more "yolk-nuclei" in addition to the "attraction-sphere" ("vitelline body" of Munson). In the second place there seem to be two well-defined modes of origin of the yolk-nucleus. In one type, illustrated by Jordan's observations on the newt ('93), the "yolk-nuclei" arise separately *in situ* in the cytoplasm without direct relation to the nucleus. The same is true of the small peripheral "yolk-nuclei" of *Limulus* (Munson). In a second and more frequent type the "yolk-nucleus" first appears very near to or in contact with the nucleus, suggesting that the latter is directly concerned in its formation. The latter is the case, for example, in the eggs of *Cymatogaster* (Hubbard, '94) *Syngnathus* (Henneguy, '96), the earthworm (Calkins, '95, Foot, '96), *Polyzonium* and other myriapods (Nemec, '97, Van Bambeke, '98), *Limulus* (Munson, '98), *Cypris* (Woltereck, '98), and *Molgula* (Crampton, '99). In nearly all of these forms the yolk-nucleus first appears in the form of a cap closely applied to one side of the nucleus (Figs. 80, 81), sometimes so closely united to the latter that it is difficult to trace a boundary between them. At a later period the yolk-nucleus moves away from the nucleus and in most, if not in all, cases breaks up into smaller and smaller fragments which contribute, directly or indirectly, to the cytoplasmic growth. In all these cases the history of the yolk-nucleus is such as to indicate the participation of the nucleus in its formation. Calkins ('95) endeavours to show that the yolk-nucleus in *Lumbricus* is directly derived from the nucleus by a casting out of a portion of the chromatin-reticulum — a result agreeing in principle with earlier observations on other eggs by Balbiani, Henneguy, Leydig, Will, and other observers. This conclusion rests partly on the apparent direct continuity of yolk-nucleus and chromatin, partly on the staining-reactions. Thus when treated with the Biondi-Ehrlich mixture (basic methyl-green, acid red fuchsin), the yolk-nucleus at first stains green like the chromatin, while the cytoplasm is red, and this is the case

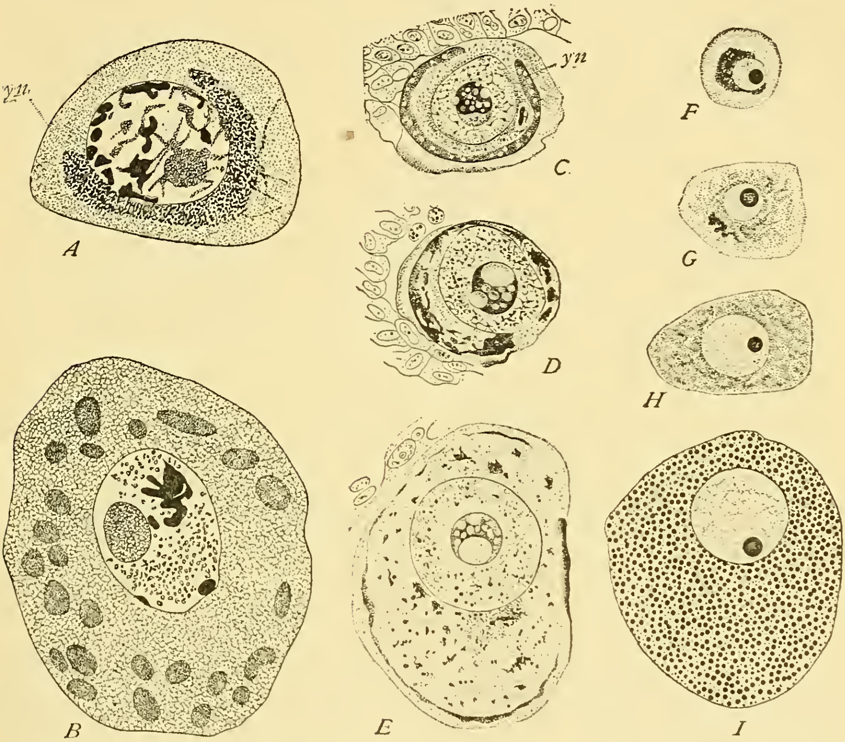

Fig. 80.—Yolk-nucleus in earthworm, spider, and ascidian. [*A*, *B*, CALKINS; *C–E*, VAN BAMBEKE; *F–I*, CRAMPTON.]

A. Early ovarian egg of *Lumbricus*. *B*. Later stage; fragmentation of yolk-nucleus. *C*. Ovarian egg of *Pholcus*. *D*. Later stage; disintegration of yolk-nucleus. *E*. Remains of the yolk-nucleus scattered through the cytoplasm. *F*. Early stage of yolk-nucleus in *Molgula*. *G–I*. Disintegration of the yolk-nucleus and enlargement of the products to form deutoplasm-spheres.

even after the yolk-nucleus has quite separated from the nuclear membrane. Later, however, as the yolk-nucleus breaks up, it changes its staining power, and stains red like the cytoplasm. The later observations of Miss Foot ('96) give ground to doubt the conclusion that the yolk-nucleus is here actually metamorphosed chromatin, for by the combined action of lithium carmine and Lyons blue its substance is sharply differentiated from the chromatin. Still later studies by Crampton ('99) on *Molgula* demonstrate that in this case the yolk-nucleus is not directly derived from chromatin, but they nevertheless indicate clearly the formation of the yolk-nucleus by or under the immediate influence of the nucleus — a conclusion also reached on less satisfactory evidence by Hubbard, Van Bambeke, Woltereck, and Nemec. The general morphological history of the yolk-nucleus is here closely similar to that of *Lumbricus* (Fig. 80), except that no direct continuity between it and the nuclear substance was observed. Stained with methyl-green-fuchsin the yolk-nucleus and major part of the nuclear substance stain red, while the scattered nuclear chromatin-granules and the cytoplasm stain green. Millon's test, combined with digestion-experiments and the foregoing staining-reactions, proves that the yolk-nucleus and the red staining nuclear substance consist of albuminous substance and differ widely from the general cytoplasm, which probably consists largely of nucleo-albumins (*cf.* p. 331). These reactions give strong ground for the conclusion that the substance of the yolk-nucleus, which progressively accumulates just outside the egg-nucleus, is formed through the direct activity of the latter, perhaps arising within the nucleus and passing out into the cytoplasm. It is possible, further, that even the scattered "yolk-nuclei" that seem to be of purely cytoplasmic origin may arise in a similar manner, either, as Crampton suggests, through the early formation and breaking up of a single yolk-nucleus, or in some less obvious way.

Interesting questions are suggested by those "yolk-nuclei," such as occur in *Geophilus* and *Limulus*, that so closely simulate an attraction-sphere. Munson's observations show that this body ("vitelline body") first appears in the very young ova as a crescent applied to the nucleus precisely as in *Molgula* or *Lumbricus*, but containing one or more central granules (Fig. 81). In later stages it becomes spherical, moves away from the nucleus, and assumes the form of a typical radial attraction-sphere with concentric microsome-circles and astral rays. It is hardly possible to doubt that this body in *Limulus* is of the same general nature as the yolk-nucleus of *Lumbricus*, *Molgula*, *Cypris*, *Cymatogaster*, or *Pholcus*; and if it be a true attraction-sphere in the one case we must probably so regard it in all. This identification is, however, by no means complete;

and even Munson's careful studies do not seem definitely to establish its connection with the attraction-sphere or centrosome of the last oögonium-division. That a body simulating an attraction-sphere and containing a central granule may arise *de novo* in the cytoplasm is shown by Lenhossék's observations on the spermatids of the rat (p. 170); and the central granule is in this case certainly not a centrosome, since the true centrosomes are found in another part of the cell. It is quite possible that the "vitelline body" of *Limulus* may have a similar origin. Nemec ('97) finds in *Polyzonium* in the earliest stages a single body applied to the nucleus and later two bodies, one of which enlarges to form a cap-shaped yolk-nucleus like those described above, while the other assumes the structure of a radiating attraction-sphere containing a central granule (centrosome ?), and his observations suggest that the two bodies in question may have a common origin (Fig. 81). In none of these cases do the astral radiations, surrounding this body, seem to have any connection with cell-division, and it is probable that a careful comparison of their physiological significance here, in leucocytes, and in mitotic division, may give us a better understanding of the general significance of astral formations in protoplasm.

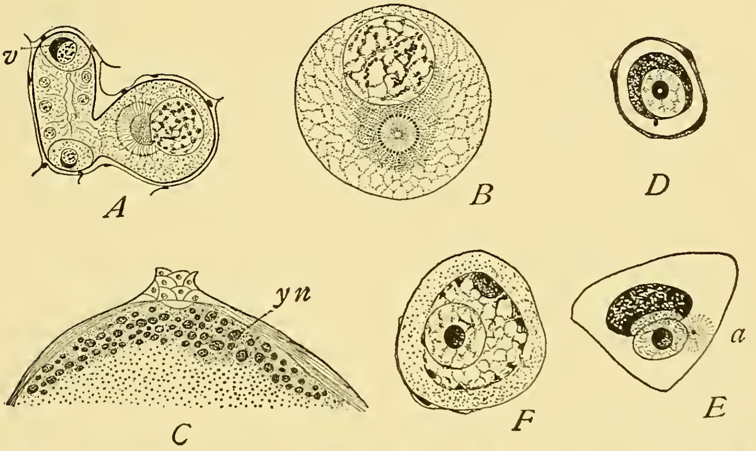

Fig. 81. — Forms of yolk-nuclei in *Limulus* and *Polyzonium*. [*A–C*, MUNSON; *D–F*, NEMEC.]

A. Very young ovarian eggs of *Limulus*; at the left "vitelline body" (*v*) in the form of a cap on the nucleus; at the right older egg showing astral formation. *B.* Older stage of the same; "vitelline body" in the form of an attraction-sphere with central granule. *C.* Peripheral "yolk-nuclei" (*y.n.*) in *Limulus*. *D.* Very early ovarian egg of a myriapod, *Polyzonium*, with yolk-nucleus. *E.* Older egg with yolk-nucleus and astral body (*a*). *F.* Still later stage, beginning disintegration of the yolk-nucleus.

The fate and physiological significance of the yolk-nucleus are still to a considerable extent involved in doubt. In many cases it breaks up into smaller and smaller granules (*Lumbricus*, *Molgula*, *Pholcus*, some myriapods, *Antedon*), which scatter through the cytoplasm and are believed by many observers (Balbiani, Mertens, Will, Calkins, Crampton, Nemec), following the earlier views of Allen Thomson, to become directly converted into deutoplasm-spheres (Fig. 80). Other observers (Van Bambeke, Foot, Stuhlman, and others) adopt the original view of Siebold, that the fragments of the yolk-nucleus are absorbed or converted into protoplasmic elements and thus only indirectly contribute to the yolk. In still other cases (*e.g.* the "vitelline body" of *Limulus*) the yolk-nucleus does not fragment, but seems to serve as a centre about which new deutoplasmic material is formed. A review of the general subject shows that we are justified only in the somewhat vague conclusion that the yolk-nucleus is probably involved in some manner in the general cytoplasmic growth; and that the facts strongly suggest, though they hardly yet prove, that at least some forms of yolk-nuclei are products of the nuclear activity and form a connecting link between that activity and the constructive processes of the cytoplasm. That the yolk-nuclei have no very definite morphological value, and that they are not necessary to growth, seems to be shown by Henneguy's observation, that in the eggs of vertebrates it is in some forms invariably present, in others only rarely, and in still others is quite wanting ('96, p. 162). If this be the case, we must conclude that the yolk-nucleus consists of material that contributes to the constructive process, but is not necessarily localized in a definite body. As to its exact *rôle* we are, as Henneguy has said, reduced to mere hypotheses.[1] The facts indicate that this material is a product of the nuclear activity, and that it may in some cases contribute directly to formed elements of the cytoplasm. It is probable, however, that beyond this the yolk-nucleus may supply materials, perhaps ferments, that play a more subtle part in the constructive process, and of whose physiological significance we are quite ignorant. The whole subject seems a most interesting and important one for further study of the actions of the cell in constructive metabolism, and it is to be hoped that further research will place the facts in a clearer light.

2. *Origin of the Spermatozoön*

(*a*) *General.* — The relation of the various parts of the spermatozoön to the structures of the spermatid is one of the most interesting questions in cytology, since it is here that we must look for a basis of interpretation of the part played by the spermatozoön in fertilization. Obviously the most important of the questions, thus suggested, is the source of the sperm-nucleus and centrosome, though the relation of the other parts to the spermatid-cytoplasm involves some interesting problems.

---

[1] '96, p. 170.

Owing to the extreme minuteness of the spermatozoön, the changes involved in the differentiation of its various parts have always been, and in some respects still remain, among the most vexed of cytological questions. The earlier observations of Kölliker, Schweigger-Seidel, and La Valette St. George, already mentioned, established the fact that the spermatozoön is a cell; but it required a long series of subsequent researches by many observers, foremost among them La Valette St. George himself, to make known the general course of spermatogenesis. This is, briefly, as follows: From the primordial germ-cells arise cells known as *spermatogonia*,[1] which at a certain period pause in their divisions and undergo a considerable growth. Each spermatogonium is thus converted into a *spermatocyte*, which by two rapidly succeeding divisions gives rise to four spermatozoa, as follows.[2] The primary spermatocyte first divides to form two daughter-cells known as spermatocytes of the second order or sperm-mother-cells. Each of these divides again — as a rule, without pausing, and without the reconstruction of the daughter-nuclei — to form two *spermatids* or sperm-cells. Each of the four spermatids is then directly transformed into a single spermatozoön, its nucleus becoming very small and compact, its cytoplasm giving rise to the tail and to certain other structures. The number of chromosomes entering into the nucleus of each spermatid and spermatozoön is always one-half that characteristic of the tissue-cells, and this reduction in number is in most, if not in all, cases effected during the two divisions of the primary spermatocyte. The reduction of the chromosomes, which is the most interesting and significant feature of the process, will be considered in the following chapter, and we are here only concerned with the transformation of the spermatid into the spermatozoön.

All observers are now agreed that the nucleus of the spermatid is directly transformed into that of the spermatozoön, the chromatin becoming extremely compact and losing, as a rule, all trace of its reticular structure. It is further certain that in some cases at least the spermatid-centrosome passes into, or gives rise to, a part of the middle-piece, and that from it the axial filament grows out into the tail. The remaining structures arise, as a rule, from the cytoplasm, and both the acrosome and the envelope of the axial filament often show a direct relation to the remains of the achromatic figure ("archoplasm" or "kinoplasm") which is found in the spermatid in the form of a sphere (sometimes an attraction-sphere) or "Nebenkern" or both. Apart from the nuclear history, these facts have been definitely determined in only a few cases, and much confusion still exists in the accounts of different observers. Thus a number of investigators (*e.g.* Platner, Field, Benda, Julin, Prenant, Niessing) have asserted that the centrosome passes into the acrosome, instead of the middle-piece — a result which stands in contradiction with the fact that during fertilization in a large number of accurately known cases the centrosome arises from or in immediate relation to the middle-piece (Amphibia, echinoderms, tunicates, annelids, mollusks, insects, etc.; see p. 212). The clearest and most positive evidence on this question, afforded by recent observations on the spermatogenesis of insects, annelids, mollusks, Amphibia, and mammals, leaves, however, little doubt that the former result was an error and that, as the facts

---

[1] The terminology, now almost universally adopted, is due to La Valette St. George. *Cf.* Fig. 118.

[2] See Fig. 119.

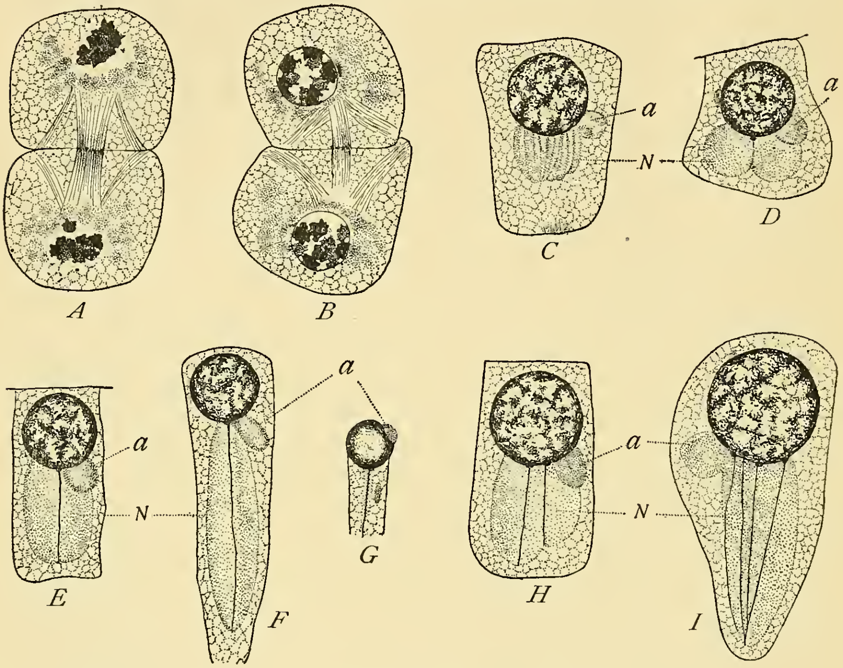

Fig. 82. — Formation of the spermatozoön in an insect, *Anasa*. [PAULMIER.]

A. Telophase of secondary spermatocyte-division, showing extra chromosome (small dyad of Fig. 127) below. *B*. Reconstitution of the nuclei. *C*. Spermatid with Nebenkern (*N*) and acrosome (*a*). *D*. Nebenkern double, with centrosome between the two halves. *E*. *F*. *G*. Elongation of the spermatid, outgrowth of axial filament, migration of acrosome. *H*. Giant spermatid (double size) with two centrosomes and axial filaments. *I*. Giant spermatid (quadruple size) with four centrosomes and axial filaments.

of fertilization would lead us to expect, the centrosome of the spermatid passes into the middle-piece.

Accounts vary considerably regarding the origin of the acrosome, which according to most authors is of cytoplasmic origin, while a few describe it as arising inside or from the anterior part of the nucleus.

(*b*) *Composition of the Spermatid.* — The confusion that has arisen in this difficult subject is owing to the fact that the spermatid may contain, besides the nucleus and centrosome, no less than three additional bodies, which were endlessly confused in the earlier studies on the subject. These are the *Nebenkern*,[1] the attraction-sphere or *idiozome* (Meves), and the *chromatoid Nebenkörper* (Benda).

The Nebenkern (Fig. 82), first described by Bütschli ('71) in the spermatids of butterflies, was afterward shown by La Valette ('86), Platner ('86, '89), and many later investigators to arise wholly or in part from the *remains of the spindle* of the second spermatocyte division. Its origin is thus related to that of an attraction-sphere (which it often closely simulates), since the latter likewise arises from the achromatic figure. To the remains of the spindle, however, may be added granular elements, probably forming reserve-material ("centro-deutoplasm of Erlanger), that are scattered through the cytoplasm or aggregated about the equator of the spindle (Fig. 126). Thus the Nebenkern may have a double origin, though its basis is formed by the spindle-remains. The Nebenkern sometimes takes a definite part in the formation of the tail-envelopes and of the acrosome (insects), but in many cases it seems to be wholly wanting.[2] The idiozome is in some cases an undoubted attraction-sphere derived from the aster of the last division and at first containing the centrosome, *e.g.* in the earthworm as shown by Calkins ('95) and Erlanger ('96, 4), in the salamander and guinea-pig, Meves ('96, '99), and in *Helix* according to Korff ('99), though in later stages the centrosomes usually pass out of the body of the idiozome. In some cases, however (in the rat, according to Lenhossék, '99), the idiozome seems to arise independently through condensation of the cytoplasmic substance into a sphere having no relation to the centrosomes. In some cases the idiozomes of adjoining cells remain for a time connected by bridges of material (Fig. 7) representing the remains of the spindle, and hence corresponding to a Nebenkern (*e.g.* salamander, Meves, '96), and the distinction between Nebenkern and idiozome here fades away. The idiozome is usually concerned in the formation of the acrosome (Amphibia, mammals), but sometimes seems to degenerate without contributing directly to the sperm-formation (*Helix*). The chromatoid Nebenkörper, finally, is a small rounded body, staining with plasma-stains, which appear always to degenerate without taking direct part in the formation of the spermatozoön. It is possibly an extruded nucleolus (Lenhossék), but its origin and meaning are not definitely known.

---

[1] The English equivalent of this should be *paranucleus*, but the latter word has already been used in various other senses, and it seems preferable to retain Bütschli's original German word.

[2] For critical discussion, see Erlanger, '97, 1.

(*c*) *Transformation of the Spermatid into the Spermatozoön.*—In the works of earlier authors it is often impossible to distinguish which of the various achromatic elements mentioned above have been under observation. We may therefore confine ourselves mainly to the latest works, in which these distinctions are clearly recognized. Owing to their great size, the spermatozoa of Amphibia have been the subject of most careful study; yet a clearer view of the subject

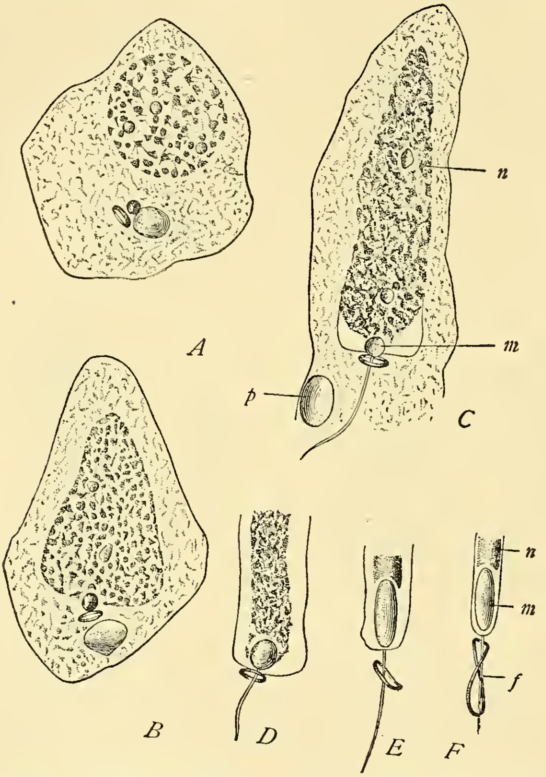

Fig. 83.—Formation of the spermatozoön from the spermatid in the salamander. [HERMANN.]

A. Young spermatid, showing the nucleus above, and below the colourless sphere, the ring, and the chromatic sphere. *B*. Later stage, showing the chromatic sphere and ring at the base of the nucleus. *C. D. E. F.* Later stages, showing the transformation of the chromatic sphere into the middle-piece (*m*).

may, perhaps, be obtained by taking the spermatogenesis of annelids and insects as a basis of comparison. In the insects (butterflies), Bütschli showed, in 1871, that the tail is formed by an elongation of the cell-body, into which extends the elongated Nebenkern, now divided into two longitudinal halves (Fig. 82). Platner ('89), confirming this observation, further showed that the Nebenkern (in *Pygæra*) consisted of two parts, stating that one ("large mitosome") gives rise to the investment of the axial filament, the other ("small mitosome") to the middle-piece; while a third still smaller body, described as a "centrosome," passes to the apex. The later works of Henking ('91) and Wilcox ('95, '96) render it nearly certain that Platner confused the acrosome with the centrosome, the first-named observer finding in *Pyrrhocoris* and the second in *Caloptenus* that Platner's "centrosome" is derived from the Nebenkern, while Wilcox traced the centrosome directly into the middle-piece. Paulmier, finally, has shown in *Anasa* that the axial filament grows out from the centrosome,[1] proving that such is the case by the highly interesting observation that in giant spermatozoa, arising by the non-division of the primary or secondary spermatocytes, either two or four centrosomes are present, each of which gives rise to a single axial filament, though only one Nebenkern is present (Fig. 82). (The bearing of this important fact on the centrosome-question is indicated elsewhere.) These observations, made on three widely different orders of insects, seem to leave no doubt that in insects the centrosome lies in the middle-piece (*i.e.* at the base of the nucleus), while both the acrosome and the inner tail-envelopes are derived from the Nebenkern. The outer envelope of the tail is derived from unmodified cytoplasm.

In the earthworm the phenomena are slightly different, the middle-piece arising from an idiozome or attraction-sphere (Calkins, '95), in which lies the centrosome (Erlanger, '96), while the Nebenkern seems to have no part in the formation of either acrosome or tail-envelopes.[2]

We turn now to the Amphibia, elasmobranchs, and mammals, in which the same general result has been attained, though there is still some divergence of opinion regarding the exact history of the centrosome. Working on the basis laid by Flemming ('87, '88), Hermann ('89) traced the middle-piece in the salamander to a "Nebenkörper," which he believed to be not a Nebenkern but an attraction-sphere, consisting of three parts, lying side by side in the cytoplasm (Fig. 83). These are (*a*) a colourless sphere, shown by Meves's later researches to be probably an attraction-sphere; (*b*) a minute, intensely staining corpuscle, and (*c*) a small, deeply staining ring. The concurrent results of Hermann ('89, '92, '97), Benda ('93), and Meves ('96, '97, 2) have shown that the small corpuscle (*c*) *is one of the centrosomes of the spermatid*, and all these observers agree that it passes into or gives

---

[1] Moore ('95) seems to have been the first actually to describe the outgrowth of the axial filament from the centrosome, in the elasmobranchs. It has since been described by Meves ('97, 2) and Hermann ('97) in the salamander, by Lenhossék ('97), Meves ('98, '99), and Bardeleben ('97) in the rat, guinea-pig, and man; by Godlewski ('97) and Korff ('99) in *Helix*, and by several others.

[2] Calkins's preparations, which I have carefully examined, seem to leave no doubt that the middle-piece arises from a true attraction-sphere derived from the spindle-poles; but Erlanger believes that the granular "centrodeutoplasm" also contributes to the sphere.

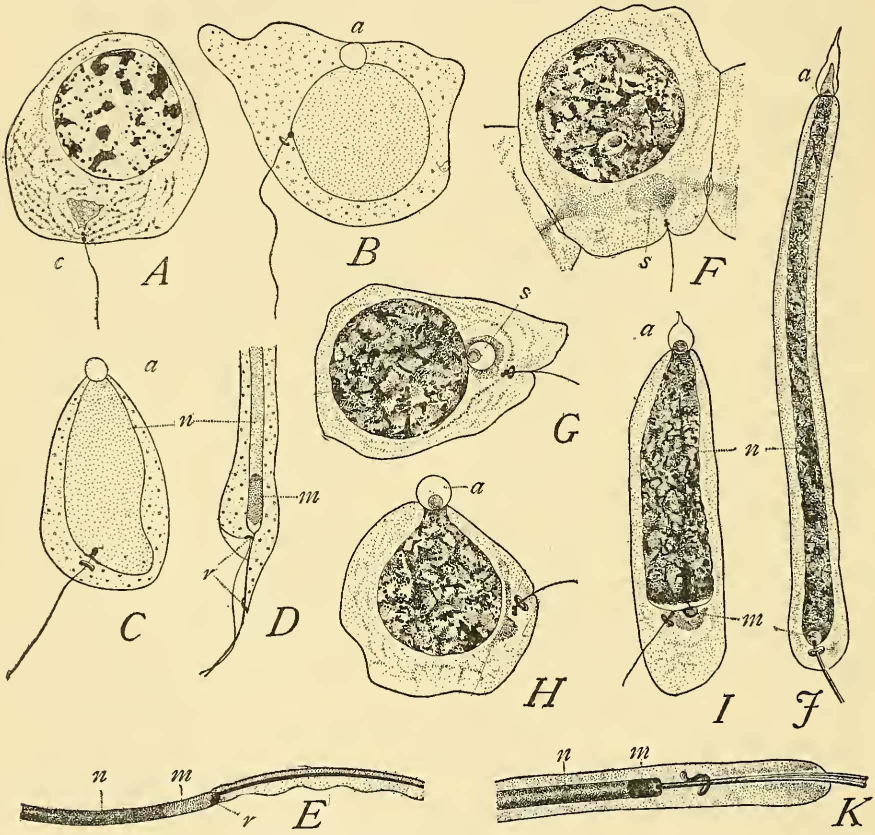

Fig. 84.—Formation of the spermatozoön in Amphibia. [*A–E. Salamandra*, Meves; *F–K. Amphiuma*, McGregor.]

A. Spermatid with peripheral pair of centrosomes lying outside the sphere, and axial filament. *B.* Centrosomes near the nucleus, outer one ring-shaped. *C.* Inner centrosome inside the nucleus, enlarging to form middle-piece. *D.* Portion of much older spermatid, showing divergence of two halves of the ring (*r*). *E.* Portion of mature spermatozoön, showing upper half of ring at *r*, and the axial filament proceeding from it.

F. Spermatid of *Amphiuma*, showing sphere-bridges and ring-shaped mid-bodies. *G.* Later stage; outer centrosome ring-shaped, inner one double; sphere (*s*) converted into the acrosome. *H.* Migration of the centrosomes. *I.* Middle-piece at base of nucleus. *J.* The inner centrosome forms the end-knob within the middle-piece, which is now inside the nucleus. *K.* Enlargement of middle-piece, end-knob within it; elongation of the ring.

rise to the middle-piece. According to Meves, who has most thoroughly studied the entire formation of the spermatozoön, the history of these parts is as follows: In the young spermatids the two centrosomes lie quite at the periphery of the cell (Fig. 84),[1] and from the outer one grows out the axial filament. The two centrosomes, leaving the idiozome by which they are first surrounded, now pass inwards toward the nucleus, the outer one meanwhile becoming transformed into the ring mentioned above, while the axial filament passes through it to become attached to the inner centrosome. The latter pushes into the base of the nucleus and enlarges enormously to form a cylindrical body constituting the main body of the middle-piece. The ring meanwhile divides into two parts, the anterior of which gives rise to a small, deeply staining body at the posterior end of the middle-piece identical with the "end-knob." The other half of the ring wanders out along the tail, finally lying at the limit between the main part of the latter and the end-piece. The envelope of the axial filament, here confined to that side opposite the marginal fin (*i.e.* the "ventral" side of Czermak), is formed by an outgrowth of the general cytoplasm along the axial filament. The fin and marginal filament are believed by Meves, as I understand him, to be formed from the axial filament ('97, 2, p. 127).[2] The acrosome, finally, is formed from the idiozome which wanders around the nucleus to its anterior pole. McGregor's results on *Amphiuma* ('99) agree in their broader features with those of Meves, but differ on two points, one of which is of great importance. The acrosome here arises from only a part of the sphere (idiozome), while a second smaller part passes to the base of the nucleus and forms the main part of the middle-piece. The inner centrosome passes into the middle-piece *to persist as the end-knob* from which the axial filament passes out into the tail (Fig. 84). The history of the sphere thus recalls the phenomena seen in the Nebenkern of the insect-spermatid; though the posterior moiety does not contribute to the tail-envelope, while the history of the inner centrosome is somewhat like that observed in the mammals, as described beyond.

In the elasmobranchs Moore ('95), Hermann ('98), Suzuki ('98), and Benda ('98) likewise traced the spermatid-centrosome into the middle-piece (Fig. 85), and Moore first showed that from it the axial filament grows out.[3] Moore derived both middle-piece and acrosome from the

---

[1] *Cf.* their position in epithelial cells, p. 57.

[2] Hermann ('97) gives a somewhat different account of the process, believing that the ring is derived from the mid-body of the last mitosis. Meves and McGregor have, however, shown that the ring and mid-body coexist in the early spermatids (Fig. 84), which seems decisive against Hermann's conclusion.

[3] Hermann finds also the ring observed in the salamander, and believes it to be the mid-body. The middle-piece is regarded by him as a product of the spindle-remains, but on both these points he is contradicted by Suzuki.

"archoplasm" of the spermatid. Suzuki's studies clearly show, however, that the entire axial filament of the long middle-piece arises by the elongation of the inner centrosome, while the outer centrosome, from which the axial filament of the tail grows out, lies at the posterior limit of the middle-piece (Fig. 85). A nearly similar result is reached by Korff ('99) in the case of *Helix*. It was shown by Godlewski ('97) that in this form the axial filament likewise grows out from the centrosome. Korff's later studies show that here, exactly as in the elasmobranch, the axial filament grows out from the peripheral centrosome and is afterward transformed into a ring (Fig. 85). The inner centrosome elongates to form a rod, which afterward becomes a long filament traversing the elongated middle-piece and terminating in front in an end-knob at the base of the nucleus, while the ring lies at its posterior limit. The idiozome (a true attraction-sphere) degenerates without taking part in the formation of an acro-

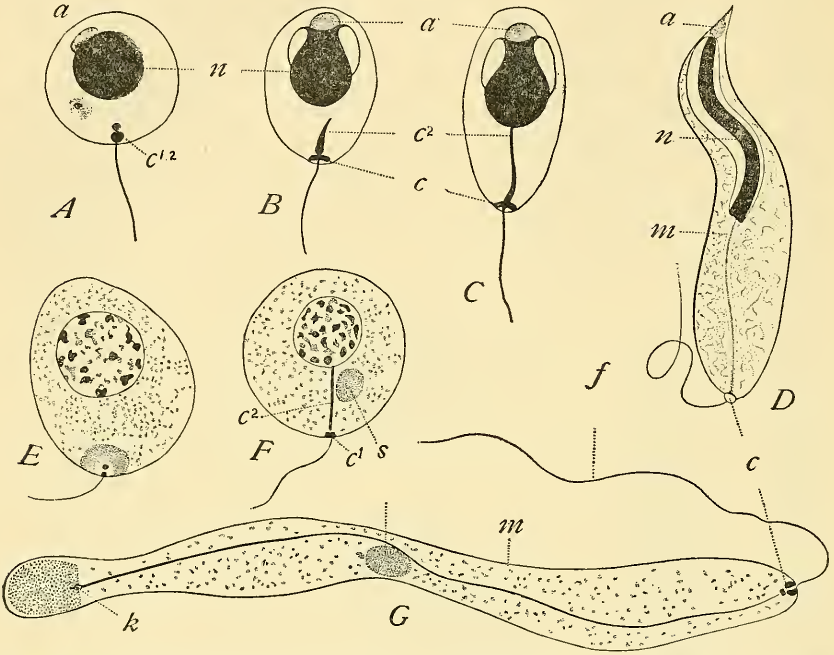

Fig. 85. — Formation of the spermatozoön in elasmobranchs. [*A–C*, Suzuki; *D*, Moore; and in *Helix*, *E–G*, Korff.]

A–D. Outgrowth of axial filament from peripheral centrosome (c^1), which persists at the posterior limit of the middle-piece or connecting-piece (m). Elongation of inner centrosome (c^2) to form the axial filament of the latter. *E–G* show similar phenomena in *Helix*, with casting off of the sphere (s).

a. Acrosome; c^1. peripheral, and c^2. inner centrosome; *f.* flagellum; *k.* end-knob, derived from inner centrosome.

some. The envelope of the middle-piece is here formed out of the general cytoplasm.

In the mammals the recent work of Lenhossék on the rat ('98) and Meves on the rat, guinea-pig, and man ('98, '99) gives a result agreeing in its broader features with the forms already considered. In all these mammals the young spermatids are closely similar to those of the salamander, containing two peripherally placed centrosomes, from the outer one of which the axial filament grows out (Fig. 86). Meves and Lenhossék differ somewhat in their accounts of the later history of these centrosomes, though agreeing that both contribute to the formation of the middle-piece. Lenhossék states that in the rat both centrosomes persist at the base of the nucleus to form the end-knob, which, as Jensen showed ('87), is double in this animal. Meves finds the process to be more complicated, agreeing in the main with that observed by him in the salamander. In man and the rat the inner centrosome passes to the base of the nucleus and flattens against it to form a small disc-shaped body. The posterior centrosome divides

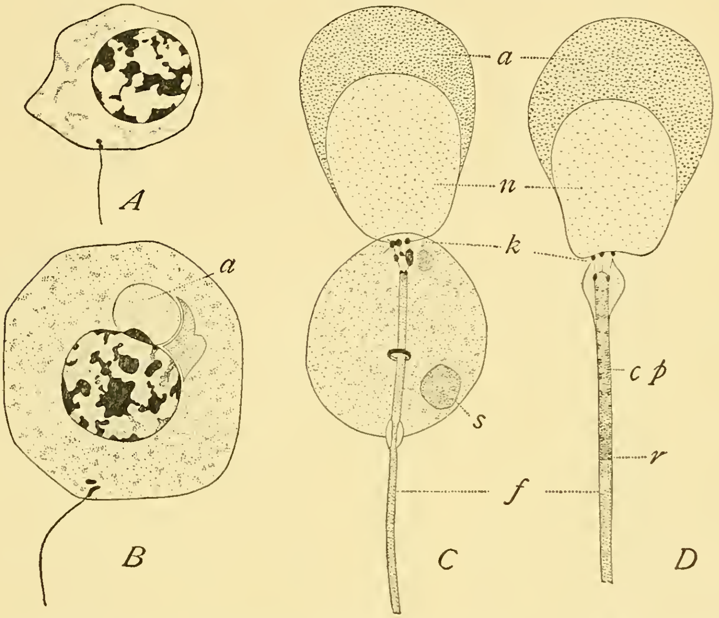

Fig. 86. — Formation of the spermatozoön in mammals. [Meves.]

A. Spermatid of man, showing centrosomes and axial filament. *B.* Spermatid of guinea-pig, with acrosome. *C.* Nearly mature spermatozoön, showing backward migration of the ring. *D.* Mature spermatozoön; *r.* final position of the ring.

a. Acrosome surrounded by cytoplasm of the cell-body, most of which is afterward thrown off; *c.* centrosomes; *c.p.* connecting-piece; *f.* flagellum; *k.* neck, containing end-knobs; *s.* remains of the sphere (idiozome).

into two parts, of which the anterior gives rise to the end-knob, while the posterior is transformed into a ring, which wanders back to its final position at the posterior end of the so-called "connecting-piece." From this it follows that the latter body (Verbindungsstück) does not correspond to the middle-piece of the salamander (here represented by the small disc-shaped body at the base of the nucleus), but belongs to the flagellum proper. The origin of the axial filament and end-knob is, however, nearly the same in the two cases. In the guinea-pig the process is somewhat more complicated and is not quite cleared up by Meves; but the origin and fate of the ring is the same, and the end-knob passes into the neck of the spermatozoön as in the rat. Taken together, these observations conclusively show that in mammals and Amphibia the end-knob is a derivative of the centrosome, thus sustaining, though with some modifications, Hermann's earlier conjecture ('92) as to the nature of this body; and they overturn Niessing's result ('96) that the centrosome passes into the acrosome. As in the salamander, the acrosome is formed from an idiozome derived in the guinea-pig from the remains of the attraction-sphere (Meves), while in the rat, according to Lenhossék, it is independently formed in the cytoplasm without relation to the preceding mitotic figure or the centrosomes. Within the sphere appears a small, deeply staining body, resembling a centrosome, yet staining differently from the true centrosome, which enlarges to form the acrosome, while about it is formed a clear substance forming the "head-cap" (p. 139). In the rat the acrosome remains small ("Spitzenknöpfchen" of Merkel); in the guinea-pig it becomes nearly as large as the nucleus itself (Fig. 86). An interesting feature in the formation of the mammalian spermatozoön is the casting off of a portion of the spermatid-cytoplasm in the form of a "cytoplasmic vesicle" or "tail-vesicle," which degenerates without further use (Fig. 86). This process, described by Meves ('99) in the guinea-pig, is closely similar to that which occurs in the spermatozoid-formation in ferns (p. 144).

Résumé. In reviewing the foregoing facts we find, despite many variations in detail, three points of fundamental agreement, namely: (1) the origin of the sperm-nucleus from that of the spermatid; (2) the origin of a part at least of the "middle-piece" from the spermatid-centrosomes; and (3) the outgrowth of the axial filament from one of the spermatid-centrosomes. It is clear, however, that the term *middle-piece* has been applied to structures of quite different morphological nature, which agree only in lying behind the nucleus. Thus in the salamander the inner centrosome gives rise to the main body of the middle-piece; in the rat or in man it gives rise only to the small disc-shaped body lying in the "neck" in front of the so-called middle-piece; while in *Helix* or the elasmobranch it is transformed into a long filament traversing a cytoplasmic "middle-piece" which forms a considerable part of the flagellum. The term *middle-piece* has thus become highly ambiguous and should only be employed, if at all, as a convenient descriptive term which has no definite morphological meaning.

A very striking fact in the origin of the spermatozoön is the prominent part played by the "archoplasm," *i.e.* substance in the form of idiozome or Nebenkern derived from the mitotic figure. Both the source and the fate of this material seem, however, to vary in different cases, the acrosome now arising from the Nebenkern (insects), now from the idiozome (salamander), the envelope of the flagellum being formed in some cases from the Nebenkern (insects), in others from unmodified cytoplasm (salamander, snail), while the idiozome may form the acrosome (salamander, mammal) or degenerate without apparent use (snail). We find here, I think, additional reason for regarding "archoplasm" not as a distinct and permanent form of protoplasm, but only as a phase in the general metabolic transformation of the cell-substance, which may or may not persist and play a definite morphological *rôle* in the cell according to circumstances. The close relation of this substance to the motor phenomena of the cell cannot, however, be overlooked.[1]

The outgrowth of the axial filament from the centrosome is a highly interesting fact, whether we compare it with the analogous phenomena in plants (p. 172) or with the facts observed in ordinary ciliated cells. In the latter case (Fig. 17), as has long been known, each cilium is attached to a small, highly refracting body known as the "basal knob" lying near the cell-periphery. These bodies stain intensely in iron hæmatoxylin, and it has been recently suggested by Henneguy ('98) and Lenhossék ('98) that they are of the same nature as centrosomes. The truth of this surmise must be tested by further study; but it seems highly probable that they are at least analogous to the spermatid-centrosome. Ishikawa ('99) has clearly shown that in the formation of the swarm-spores of *Noctiluca* the flagellum grows out from that end of the cell at which the centrosome lies, its substance apparently arising from the central spindle, while the centrosome lies at its base. A very interesting fact discovered by Moore ('95) in elasmobranchs, and confirmed by Meves ('97, 5) and Henneguy ('98) in the insects, is a more or less abortive attempt to form a flagellum by the spermatocytes, *i.e.* one or two generations before the spermatozoön. In the insects (Fig. 166) Henneguy has found the cilia actually attached to the centrosomes of the mitotic figure, thus removing every doubt as to their nature.[2]

---

[1] *Cf.* 323.

[2] *Cf.* Paulmier on giant spermatozoa, p. 165.

It is an important question whether the axial filament actually arises from the substance of the centrosome or is formed by differentiation from the cytoplasmic substance, after the fashion of an astral ray or spindle-fibre. Meves ('97, p. 117) accepts the latter alternative; but the observations of Korff on *Helix* and of Suzuki on elasmobranchs seem to show clearly that, in these cases at least, the inner centrosome elongates bodily to form an extremely long filament traversing the greater part of the flagellum, and apparently of the same nature as the true axial filament developed from the outer or distal centrosome. This seems to establish a probability in favour of the first of the above alternatives, and to show that contractile elements may be directly derived from the centrosome-substance. If this be true, this substance is itself nearly related with "archoplasm"; and the origin of a centrosome *de novo* may be brought under the same category with the formation of archoplasm.[1]

3. *Formation of the Spermatozoids in Plants*

While the origin of the spermatozoids has not yet been as fully investigated as that of the spermatozoa, recent researches have given good ground for the conclusion that essentially similar phenomena are involved in the two cases. All recent observers are agreed that the nucleus of the spermatozoid is directly derived from that of the spermatid, while the cytoplasm of the latter gives rise to the cilia and to certain other structures. The principal interest of the subject now lies in the origin of the cilia and their relation to the "archoplasmic" or "kinoplasmic" structures of the mother-cell. Belajeff ('92, '94) found that in *Chara* the cilia grow forth from a small, highly refracting body, taking an intense plasma-stain, that lies in the cytoplasma beside the nucleus. He afterward found the same body "which reminds one of a centrosome" in the developing spermatozoids of ferns and Equisetaceæ (Fig. 88), where it grows out into a band, lying in the anterior part of the spermatozoid, from which the cilia grow forth. Comparing these results with those of Hermann, Belajeff concluded "that the deeply staining corpuscle" (*i.e.* the centrosome) "in the spermatids of the salamander and the mouse corresponds completely to the deeply staining corpuscle in the spermatogenic cells of the Characeæ, ferns, and Equisetaceæ"; that, furthermore, "the middle-piece of the spermatozoön represents the band which bears the cilia of the plant spermatozoid, while the tail-like flagella[2] of the salamander or mouse represents the cilia."[3]

---

[1] *Cf.* p. 321. For the function of the centrosome in fertilization, see p. 208.

[2] In the original "Fäden" perhaps meant to designate the axial filament.

[3] '97, 3.

This tallies with Strasburger's earlier conclusion that the cilia-bearing region consists of "kinoplasm" and corresponds to the middle-piece ('92, p. 139), but gives a still more definite basis of comparison.[1]

The history of the centrosome-like bodies (*blepharoplasts* of Webber, '97, 3) has been carefully followed out in *Zamia* and *Gingko* by Webber ('97), and in *Cycas* by Ikeno ('97, '98) with nearly similar results. In all these forms (Fig. 87) the blepharoplasts appear in the penultimate cell-generation lying one on either side the nucleus, and in earlier stages surrounded by astral radiations very closely resembling those of a typical mitotic aster, and they lie opposite the poles

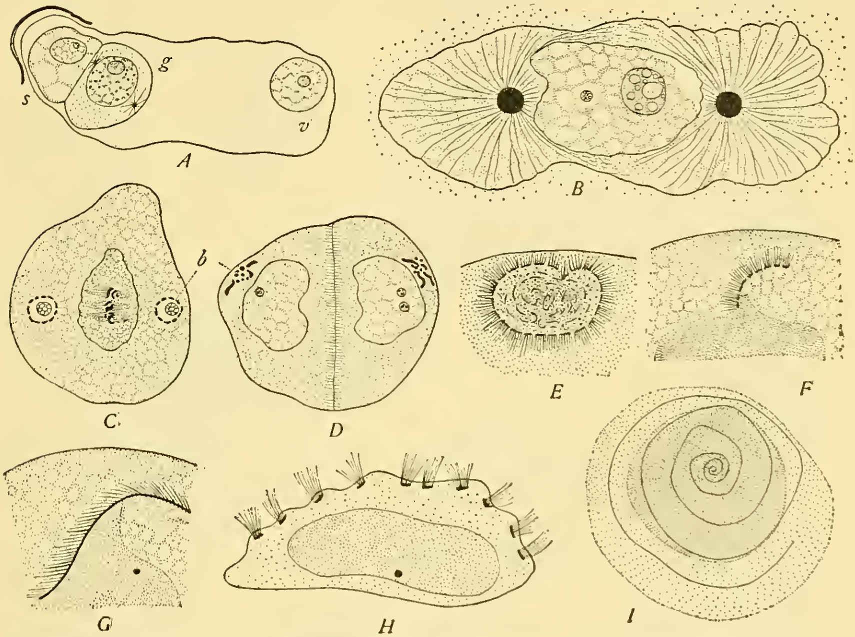

Fig. 87. — Formation of the spermatozoids in the cycads. [*A*, GINGKO; *B–D*, *Zamia*, WEBBER; *E–I*, *Cycas*, IKENO.]

A. Developing pollen-tube, showing stalk-cell (*s*), vegetative cell (*v*) and generative cell (*g*), the latter with two blepharoplasts. *B*. Generative cell, somewhat later, with blepharoplasts and asters. *C*. The same in the prophases of division, showing breaking up of blepharoplasts. *D*. The two spermatids formed by division of the generative cell; blepharoplasts fragmented; from these fragments arises the cilia-bearing band. *E*. Blepharoplast of *Cycas*, at a stage somewhat later than Fig. *C*; cilia developing. *F*. Later stage; ciliated band (derived from the last stage) attached to a prolongation from the nucleus. *G*. Cilia-bearing band continuous. *H*. Nearly ripe spermatozoid with nucleus in the centre; ciliated band, shown in section, forming a spiral. *I*. Slightly later stage, viewed from above, showing the spiral course of the band (cilia omitted).

---

[1] The "anterior" region of the spermatozoid thus corresponds to the "posterior" region of the spermatozoön, the confusion of terms having arisen from the fact that the former swims with the cilia-bearing region in front, the latter with the flagellum directed backward.

of the ensuing division-spindle. They seem, however, to have no part in the formation of the mitotic figure or in division, and both

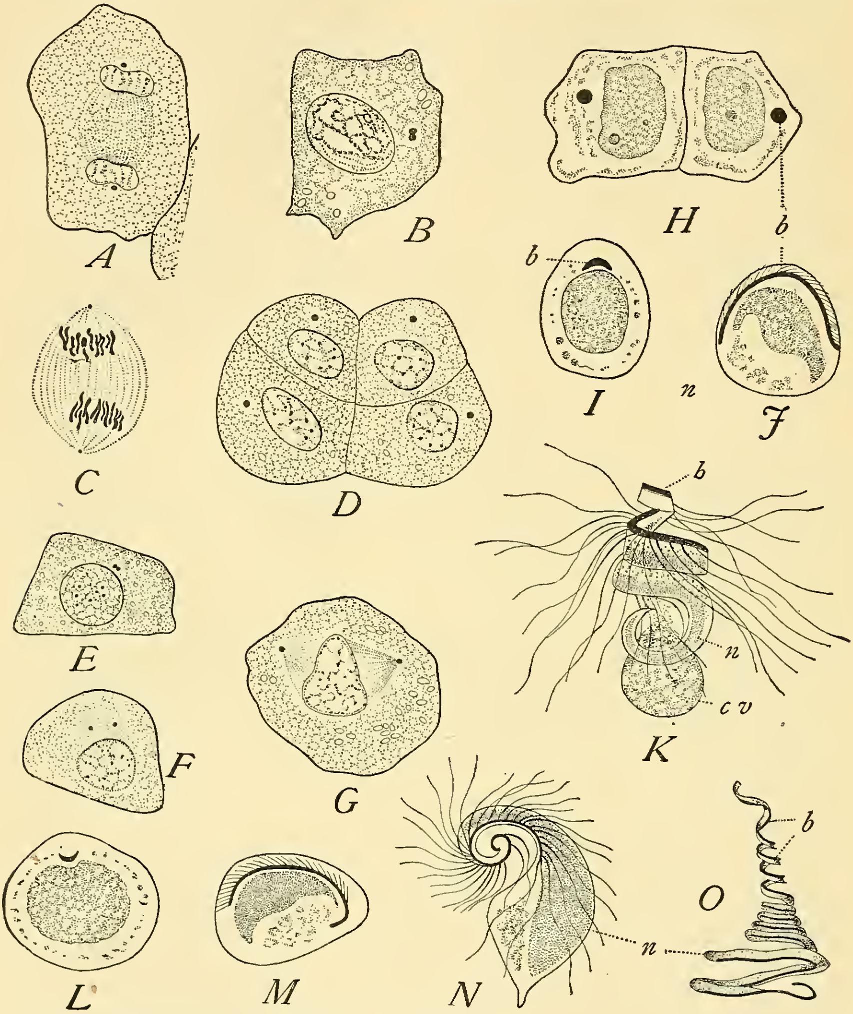

Fig. 88. — Formation of the spermatozoids in the vascular cryptogams, *Marsilia* (*A*, *D*, *E–G*, Belajeff; *B*, *C*, *O*, Shaw), *Gymnogramme* (*H–K*, Belajeff), and *Equisetum* (*L–N*, Belajeff).

A. Primary spermatogonium (two generations before the primary spermatocytes) in division, showing centrosomes. *B.* Primary spermatocyte with pair of "blepharoplastoids" (centrosomes). *C.* Spindle of primary spermatocyte (first maturation-division). *D.* Four of the eight secondary spermatocytes with blepharoplast. *E–G.* Prophase of second maturation-division. *H.* Pair of spermatids (*Gymnogramme*) with blepharoplasts. *I–J.* Formation of the ciliated band from the blepharoplast. *K.* Nearly ripe spermatozoid, showing ciliated band (*b*), nucleus, and "cytoplasmic vesicle" (the latter is ultimately cast off). *L. M.* Spermatids of *Equisetum*. *N.* Ripe spermatozoid from above, showing spiral ciliated band. *O.* Ripe spermatozoid of *Marsilia* with very long spiral ciliated band.

Webber and Ikeno have produced apparently strong evidence[1] that they arise separately and *de novo* in the cytoplasm. After the ensuing division (by which the two spermatids are formed) the astral rays disappear, and the blepharoplast gives rise by a peculiar process to a long, spiral, deeply staining band, from which the cilia grow forth. The later studies of Shaw ('98, 1) and Belajeff ('99) on the blepharoplasts in *Onoclea* and *Marsilia* leave no doubt that these bodies are to be identified with centrosomes. In *Marsilia* Shaw first found the blepharoplasts lying at the poles of the spindle during the anaphase of the first maturation-division and very closely resembling centrosomes. Each blepharoplast, at first single, divides into two during the late telophase, and during the prophases of the second division the halves diverge to opposite poles of the nucleus and lie at the respective spindle-poles. This account is confirmed by Belajeff, who shows further that during the prophases astral rays surround the blepharoplasts, and a central spindle is formed between them (Fig. 88). Belajeff also finds centrosomes in all of the earlier spermatogenic divisions. The blepharoplasts are thus proved to be, in one case at least, dividing organs which in every way correspond to the centrosomes of the animal spermatocytes; and the justice of Belajeff's comparison is demonstrated. Shaw believed that the primary blepharoplast, which by division gives rise to those of the two spermatids, arose *de novo*. He made, however, the significant observation that in *Marsilia* "blepharoplastoids," exactly like the blepharoplasts, appear at the spindle-poles of the preceding (antepenultimate) division, and that each of these divides into two in the late telophase. These are said to disappear, without relation to the blepharoplasts which at a slightly later period are found at the spindle-poles of the first maturation division; but in view of the demonstrated continuity of the blepharoplasts during the second division we may well hesitate to accept this result, as well as Webber's conclusion regarding the independent and separate origin of the blepharoplasts in *Zamia*. In any case the facts give the strongest ground for the conclusion that the formation of the spermatozoids agrees in its essential features with that of the spermatozoa, and for the expectation that the history of the achromatic structures in fertilization will yet be found to show an essential agreement in plants and animals.

E. Staining-reactions of the Germ-nuclei

It was pointed out by Ryder in 1883 that in the oyster the germ-nuclei stain differently in the two sexes; for if the hermaphrodite gland of this animal be treated with a mixture of saffranin and methyl-green, the egg-nuclei are coloured red, the sperm-nuclei bluish green. A similar difference was afterward observed by Auerbach ('91) in the case of many vertebrate germ-cells, where the egg-nucleus was shown to have a special affinity for various red and yellow dyes (eosin, fuchsin, aurantia, carmine), while the sperm-nuclei were especially stained with blue and green dyes (methyl-green, aniline-blue, hæmatoxylin). He was thus led to regard the chromatin of the egg as especially "erythrophilous," and that of the sperm as "cyanophilous." That the distinction as regards colour is of no value has been shown by Zacharias, Heidenhain, and others; for staining-agents cannot be logically classed according to colour, but according to their chemical composition; and a red dye, such as saffranin, may in a given cell show the same affinity for the chromatin as a green or blue dye of different chemical nature, such as methyl-green or hæmatoxylin. Thus Field has shown that the sperm-nucleus of *Asterias* may be stained green (methyl-green), blue (hæmatoxylin, gentian violet), red (saffranin), or yellow (iodine), and it is here a manifest absurdity to speak of "cyanophilous" chromatin (*cf.* p. 335). It is certainly a very interesting fact that a difference of staining-reaction exists between the two sexes, as indicating a corresponding difference of chemical composition in the chromatin; but even this has been shown to be of a transitory character, for the staining-reactions of the germ-nuclei vary at different periods and are exactly alike at the time of their union in fertilization. Thus Hermann has shown that when the spermatids and immature spermatozoa of the salamander are treated with saffranin (red) and gentian violet (blue),[1] the chromatic network is stained blue, the nucleoli and the middle-piece red; while in the mature spermatozoön the reverse effect is produced, the nuclei being clear red, the middle-piece blue. A similar change of staining-capacity occurs in the mammals. The great changes in the staining-capacity of the egg-nucleus at different periods of its history are described at pages 338–340. Again, Watasé has observed in the newt that the germ-nuclei, which stain differently throughout the whole period of their maturation, and even during the earlier phases of fertilization, become more and more alike in the later phases, and at the time of their union show identical staining-reactions.[2] A very similar series of facts has been observed in the germ-nuclei of plants by Strasburger (p. 220). These and many other facts of like import demonstrate that the chemical differences between the germ-nuclei are not of a fundamental but only of a secondary character. They are doubtless connected with the very different character of the metabolic processes that occur in the history of the two germ-cells; and

---

[1] Dr. Webber has kindly given me an opportunity to look through his beautiful preparations.

[1] By Flemming's triple method.

[2] '92, p. 492.

the difference of the staining-reaction is probably due to the fact that the sperm-chromatin contains a higher percentage of nucleinic acid, while the egg-chromatin is a nuclein containing a much higher percentage of albumin.

LITERATURE. III[1]

Ballowitz, E. — Untersuchungen über die Struktur der Spermatozoen: 1. (*birds*) *Arch. mik. Anat.*, XXXII. 1888; 2. (*insects*) *Zeitschr. wiss. Zool.*, L. 1890; 3. (*fishes, amphibia, reptiles*) *Arch. mik. Anat.*, XXXVI. 1890; 4. (*mammals*) *Zeit. wiss. Zool.*, LII. 1891.

Belajeff, W. — Über die Centrosomen in den spermatogenen Zellen: *Ber. d. deutsch. bot. Ges.*, XVII., 6. 1899.

Boveri, Th. — Über Differenzierung der Zellkerne während der Furchung des Eies von *Ascaris meg.*: *Anat. Anz.* 1887.

Id. — Die Entwicklung von Ascaris megalocephala mit besonderer Rücksicht auf die Kernverhältnisse: *Festschr. für C. v. Kupffer. Jena*, 1899.

Brunn, M. von. — Beiträge zur Kenntniss der Samenkörper und ihrer Entwickelung bei Vögeln und Säugethieren: *Arch. mik. Anat.*, XXXIII. 1889.

Häcker, V. — Die Eibildung bei Cyclops und Camptocanthus: *Zool. Jahrb.*, V. 1892. (See also List V.)

Hermann, F. — Urogenitalsystem: Struktur und Histiogenese der Spermatozoen: *Merkel und Bonnet's Ergebnisse*, II. 1892.

Ikeno, S. — Untersuchungen über die Entwickelung der Geschechtsorgane, *etc.*, bei Cycas: *Jahrb. wiss. Bot.*, XXXII., 4. 1898.

Kölliker, A. — Beiträge zur Kenntniss der Geschlechtsverhältnisse und der Samenflüssigkeit wirbelloser Tiere. *Berlin*, 1841.

Leydig, Fr. — Beiträge zur Kenntniss des thierischen Eies im unbefruchteten Zustande: *Zool. Jahrb.*, III. 1889.

Meves, F. — Über die Entwicklung der männlichen Geschechtszellen von Salamandra: *Arch. mik. Anat.*, XLVIII. 1896.

Id. — Über Struktur und Histogenese der Samenfäden des Meerschweinchens: *Arch. mik. Anat.*, LIV. 1899.

Schweigger-Seidel, F. — Über die Samenkörperchen und ihre Entwicklung: *Arch. mik. Anat.*, I. 1865.

Strasburger, E. — Histologische Beiträge; Heft IV.: Das Verhalten des Pollens und die Befruchtungsvorgänge bei den Gymnospermen, Schwärmsporen, pflanzliche Spermatozoiden und das Wesen der Befruchtung. *Fischer, Jena*, 1892.

Thomson, Allen. — Article "Ovum," in Todd's Cyclopedia of Anatomy and Physiology. 1859.

Van Beneden, E. — Recherches sur la composition et la signification de l'œuf: *Mem. cour. de l'Acad. roy. de Belgique.* 1870.

Waldeyer, W. — Eierstock und Ei. *Leipzig*, 1870.

Id. — Bau und Entwickelung der Samenfäden: *Verh. d. Anat. Ges. Leipzig*, 1887.

---

[1] See also Literature, V., p. 287.

CHAPTER IV

FERTILIZATION OF THE OVUM

> "It is conceivable, and indeed probable, that every part of the adult contains molecules derived both from the male and from the female parent; and that, regarded as a mass of molecules, the entire organism may be compared to a web of which the warp is derived from the female and the woof from the male." HUXLEY.[1]

IN mitototic cell-division we have become acquainted with the means by which, in all higher forms at least, not only the continuity of life, but also the maintenance of the species, is effected; for through this beautiful mechanism the cell hands on to its descendants an exact duplicate of the idioplasm by which its own organization is determined. As far as we can see from an *a priori* point of view, there is no reason why, barring accident, cell-division should not follow cell-division in endless succession in the stream of life. It is possible, indeed probable, that such may be the fact in some of the lower and simpler forms of life where no form of sexual reproduction is known to occur. In the vast majority of living forms, however, the series of cell-divisions tends to run in cycles in each of which the energy of division finally comes to an end and is only *restored by an admixture of living matter derived from another cell.* This operation, known as *fertilization* or *fecundation*, is the essence of sexual reproduction; and in it we behold a process by which on the one hand the energy of division is restored, and by which on the other hand two independent lines of descent are blended into one. Why this dual process should take place we are as yet unable to say, nor do we know which of its two elements is to be regarded as the primary and essential one.

Harvey and many other of the early embryologists regarded fertilization as a stimulus, given by the spermatozoön, through which the ovum was "animated" and thus rendered capable of development. In its modern form this conception appears in the "dynamic" theories of Herbert Spencer, Bütschli, Hertwig, and others, which assume that protoplasm tends gradually to pass into a state of increasingly stable equilibrium in which its activity diminishes, and that fertilization restores it to a labile state, and hence to one of activity, through mixture with protoplasm that has been subjected to different conditions. Bütschli ('76) pointed out that the life-cycle of the metazoön is comparable to that of a protozoan race, a long series of cell-divisions being in each case followed by a mixture of protoplasms through conjugation; and he assumed that, in both cases, conjugation results in rejuvenescence through which the energy of growth and division is restored and a new cycle inaugurated. The same view has been advocated by Minot, Engelman, Hensen, and many others. Maupas ('88, '89), in his celebrated researches in the conjugation of Infusoria, attempted to test this conclusion by following out continuously the life-history of various species through the entire cycle of their existence. Though not yet adequately confirmed, and indeed opposed in some particulars by more recent work,[1] these researches have yielded very strong evidence that in these unicellular animals, even under normal conditions, the processes of growth and division sooner or later come to an end, undergoing a process of natural "senescence," which can only be counteracted by conjugation. That fertilization in higher plants and animals does in fact incite division and growth is a matter of undisputed observation. We know, however, that in parthenogenesis the egg may develop without fertilization, and we do not know whether the tendency to "senescence" and the need for fertilization are primary attributes of living matter.

---

[1] Evolution, in *Science and Culture*, p. 296, from *Enc. Brit.*, 1878.

The foregoing views may be classed together as the rejuvenescence theory. Parallel to that theory, and not necessarily opposed to or confirmatory of it, is the view that fertilization is in some way concerned with the process of variation. Long since suggested by Treviranus and more lately developed by Brooks [2] and Weismann [3] is the hypothesis that fertilization is a source of variation — a conclusion suggested by the experience of practical breeders of plants and animals. Weismann brings forward strong arguments against the rejuvenescence-theory, and regards the need for fertilization as a secondary acquisition, the mixture of protoplasms to which it leads producing variations — or rather insuring their "mingling and persistent renewal" [4] — which form the material on which selection operates. On the other hand, a considerable number of writers, including Darwin, Spencer, O. Hertwig, Hatschek, and others, believe that although crossing may lead to variability within certain limits, its effect in the long run tends to neutralize indefinite variability and thus to hold the species true to the type.

It is remarkable that we should still remain uncertain as to the physiological meaning of a process so general and one that has been the subject of such prolonged research. Both the foregoing general views are in harmony with the results of Darwin's work on variation and with the experience of practical breeders, which have shown that crossing produces both greater vigour and greater variability. In view of all the facts, however, we are constrained to the admission that the essential nature of sexual reproduction must remain undetermined until the subject shall have been far more thoroughly investigated, especially in the unicellular forms, where the key to the ultimate problem is undoubtedly to be sought.

---

[1] *Cf.* Joukowsky, '99.

[2] The *Law of Heredity*, 1883.

[3] Amphimixis, 1891.

[4] '99, p. 326.

A. PRELIMINARY GENERAL SKETCH

Among the unicellular plants and animals, fertilization is effected by means of *conjugation*, a process in which two individuals either fuse together permanently or unite temporarily and effect an exchange of nuclear matter, after which they separate. *In all the higher forms fertilization consists in the permanent fusion of two germ-cells, one of paternal and one of maternal origin.* We may first consider the fertilization of the animal egg, which appears to take place in essentially the same manner throughout the animal kingdom, and to be closely paralleled by the corresponding process in plants.

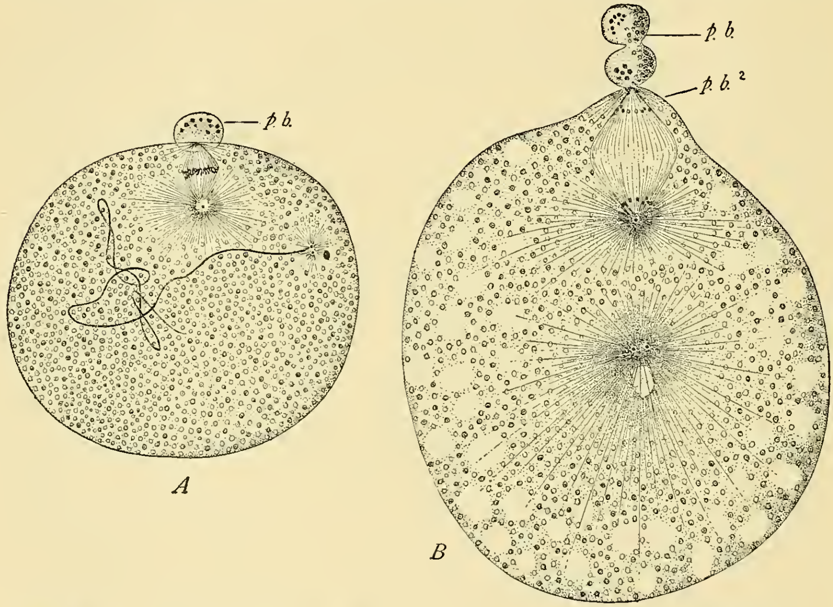

Fig. 89. — Fertilization of the egg of the snail, *Physa*. [KOSTANECKI and WIERZEJSKI.]

A. The entire spermatozoön lies in the egg, its nucleus at the right, flagellum at the left, while the minute sperm-amphiaster occupies the position of the middle-piece. The first polar body has been formed, the second is forming. *B*. The enlarged sperm-nucleus and sperm-amphiaster lie near the centre; second polar body forming and the first dividing. The egg-centrosomes and asters afterward disappear, their place being taken by those of the spermatozoön.

Leeuwenhoek, whose pupil Hamm discovered the spermatozoa (1677), put forth the conjecture that the spermatozoön must penetrate into the egg; and the classical experiments of Spallanzani on the frog's egg (1786) proved that the fertilizing element must be the spermatozoa and not the liquid in which they swim. The penetration of the ovum was, however, not actually seen until 1854, when Newport observed it in the case of the frog's egg; and it was described by Pringsheim a year later in one of the lower plants, *Œdigonium.* The first adequate description of the process was given by Hermann Fol, in 1879,[1] though many earlier observers, from the time of Martin Barry ('43) onward, had seen the spermatozoön inside the egg-envelopes, or asserted its entrance into the egg.

In many cases the entire spermatozoön enters the egg (mollusks, insects, nematodes, some annelids, *Petromyzon*, axolotl, etc.), and in such cases the long flagellum may sometimes be seen coiled within the egg (Fig. 89). Only the nucleus and middle-piece, however, are concerned in the actual fertilization; and there are some cases (echinoderms) in which the tail is left outside the egg. At or near the time of fertilization, the egg successively segments off at the upper pole two minute cells, known as the *polar bodies* (Figs. 89, 90, 116) or directive corpuscles, which degenerate and take no part in the subsequent development. This phenomenon takes place, as a rule, immediately after entrance of the spermatozoön. It may, however, occur before the spermatozoön enters, and it forms no part of the process of fertilization proper. It is merely the final act in the process of *maturation*, by which the egg is prepared for fertilization, and we may defer its consideration to the following chapter.

1. *The Germ-nuclei in Fertilization*

The modern era in the study of fertilization may be said to begin with Oscar Hertwig's discovery, in 1875, of the fate of the spermatozoön within the egg. Earlier observers had, it is true, paved the way by showing that, at the time of fertilization, the egg contains *two nuclei* that fuse together or become closely associated before development begins. (Warneck, Bütschli, Auerbach, Van Beneden, Strasburger.) Hertwig discovered, in the egg of the sea-urchin (*Toxopneustes lividus*), that *one of these nuclei belongs to the egg, while the other is derived from the spermatozoön.* This result was speedily confirmed in a number of other animals, and has since been extended to every species that has been carefully investigated. The researches of Strasburger, De Bary, Schmitz, Guignard, and others have shown that the same is true of plants. *In every known case an*

---

[1] See *l'Hénogénie*, pp. 124 ff., for a full historical account.

essential phenomenon of fertilization is the union of a sperm-nucleus, of paternal origin, with an egg-nucleus, of maternal origin, to form the primary nucleus of the embryo. This nucleus, known as the cleavage- or segmentation-nucleus, gives rise by division to all the nuclei of the body, and hence every nucleus of the child may contain nuclear substance derived from both parents. And thus Hertwig was led to the conclusion ('84), independently reached at the same time by Strasburger, Kölliker, and Weismann, that the nucleus is the most essential element concerned in hereditary transmission.

This conclusion received a strong support in the year 1883, through the splendid discoveries of Van Beneden on the fertilization of the thread-worm, *Ascaris megalocephala*, the egg of which has since ranked with that of the echinoderm as a classical object for the study of cell-problems. Van Beneden's researches especially elucidated the structure and transformations of the germ-nuclei, and carried the analysis of fertilization far beyond that of Hertwig. In *Ascaris*, as in all other animals, the sperm-nucleus is extremely minute, so that at first sight a marked inequality between the two sexes appears to exist in this respect. Van Beneden showed not only that the inequality in size totally disappears during fertilization, but that the two nuclei undergo a parallel series of structural changes which demonstrate their precise morphological equivalence down to the minutest detail; and here, again, later researches, foremost among them those of Boveri, Strasburger, and Guignard, have shown that, essentially, the same is true of the germ-cells of other animals and of plants. The facts in *Ascaris* (variety *bivalens*) are essentially as follows (Fig. 90): After the entrance of the spermatozoön, and during the formation of the polar bodies, the sperm-nucleus rapidly enlarges and finally forms a typical nucleus exactly similar to the egg-nucleus. The chromatin in each nucleus now resolves itself into two long, worm-like chromosomes, which are exactly similar in form, size, and staining-reaction in the two nuclei. Next, the nuclear membrane fades away, and the four chromosomes lie naked in the egg-substance. Every trace of sexual difference has now disappeared, and it is impossible to distinguish the paternal from the maternal chromosomes (Fig. 90, *D*, *E*). Meanwhile an amphiaster has been developed which, with the four chromosomes, forms the mitotic figure for the first cleavage of the ovum, *the chromatic portion of which has been synthetically formed by the union of two equal germ-nuclei.* The later phases follow the usual course of mitosis. Each chromosome splits lengthwise into equal halves, the daughter-chromosomes are transported to the spindle-poles, and here they give rise, in the usual manner, to the nuclei of the two-celled stage. *Each of these nuclei, therefore, receives exactly equal amounts of paternal and maternal chromatin.*

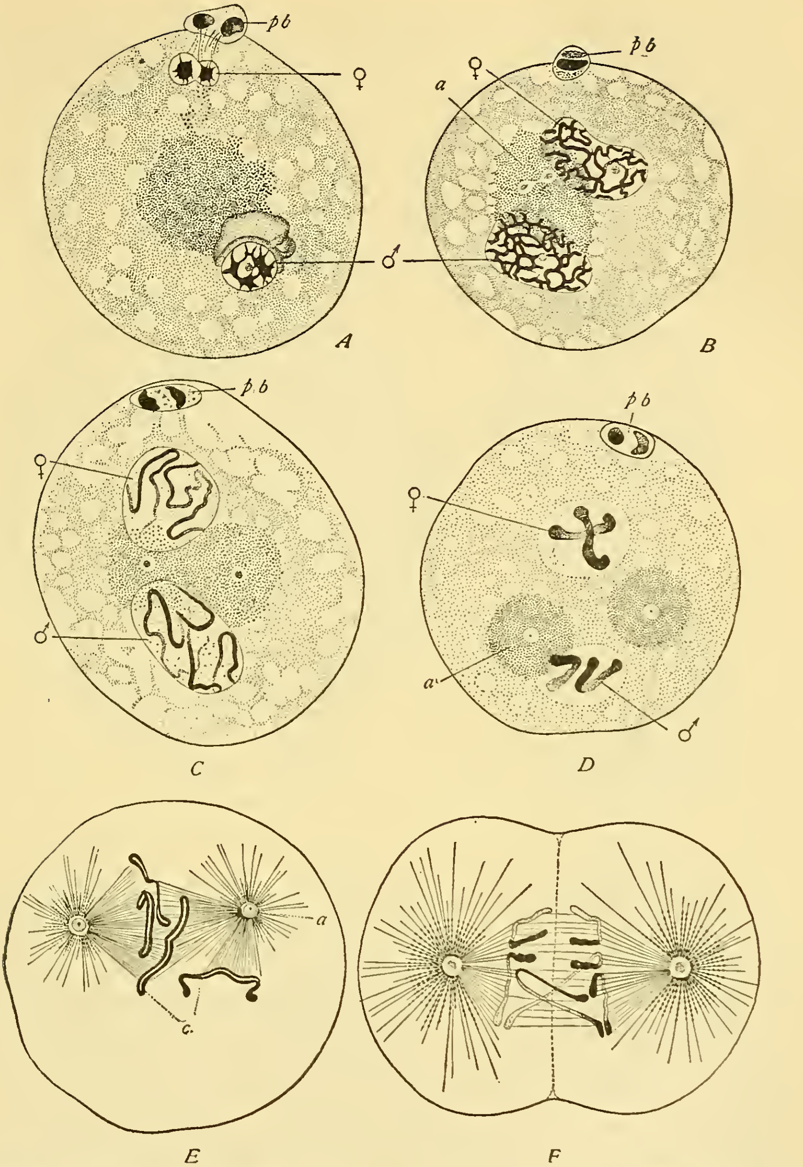

Fig. 90. — Fertilization of the egg of *Ascaris megalocephala*, var. *bivalens*. [Boveri.] (For later stages see Figs. 31, 145.)

A. The spermatozoön has entered the egg, its nucleus is shown at ♂; beside it lies the granular mass of "archoplasm" (attraction-sphere); above are the closing phases in the formation of the second polar body (two chromosomes in each nucleus). *B*. Germ-nuclei (♀, ♂) in the reticular stage; the attraction-sphere (*a*) contains the dividing centrosome. *C*. Chromosomes forming in the germ-nuclei; the centrosome divided. *D*. Each germ-nucleus resolved into two chromosomes; attraction-sphere (*a*) double. *E*. Mitotic figure forming for the first cleavage; the chromosomes (*c*) already split. *F*. First cleavage in progress, showing divergence of the daughter-chromosomes toward the spindle-poles (only three chromosomes shown).

These discoveries were confirmed and extended in the case of *Ascaris* by Boveri and by Van Beneden himself in 1887 and 1888 and in several other nematodes by Carnoy in 1887. Carnoy found the number of chromosomes derived from each sex to be in *Coronilla* 4, in *Ophiostomum* 6, and in *Filaroides* 8. A little later Boveri ('90) showed that the law of numerical equality of the paternal and maternal chromosomes held good for other groups of animals, being in the sea-urchin *Echinus* 9, in the worm *Sagitta* 9, in the medusa *Tiara* 14, and in the mollusk *Pterotrachea* 16 from each sex. Similar results were obtained in other animals and in plants, as first shown by Guignard in the lily ('91), where each sex contributes 12 chromosomes.

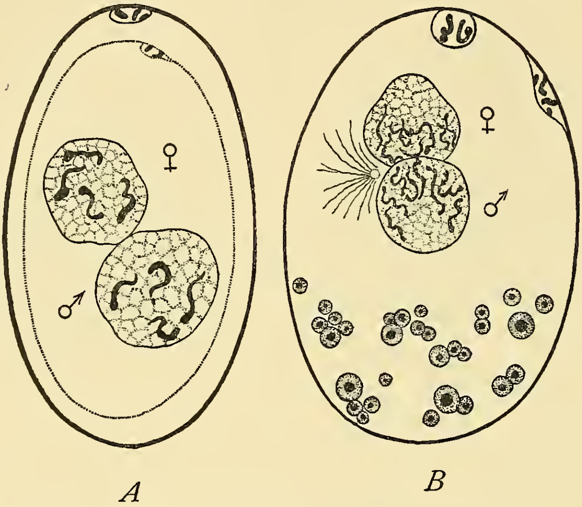

Fig. 91.— Germ-nuclei and chromosomes in the eggs of nematodes. [CARNOY.]

A. Egg of nematode parasitic in *Scyllium*; the two germ-nuclei in apposition, each containing four chromosomes; the two polar bodies above. *B.* Egg of *Filaroides*; each germ-nucleus with eight chromosomes; polar bodies above, deutoplasm-spheres below.

In the onion the number is 8 (Strasburger); in the annelid *Ophryotrocha* it is only 2 from each sex (Korschelt). In all these cases the *number contributed by each is one-half the number characteristic of the body-cells.* The union of two germ-cells thus restores the normal number, and here we find the explanation of the remarkable fact commented on at page 67 that *the number of chromosomes in sexually produced organisms is always even.*[1]

These remarkable facts demonstrate the two germ-nuclei to be in a morphological sense precisely equivalent, and they not only lend very strong support to Hertwig's identification of the nucleus as the bearer of hereditary qualities, but indicate further that these qualities must be carried by the chromosomes; for their precise equivalence in number, shape, and size is the physical correlative of the fact that the two sexes play, on the whole, equal parts in hereditary transmission.

---

[1] *Cf.* p. 67.

2. *The Achromatic Structures in Fertilization*

It is generally agreed that the amphiaster of the primary mitotic figure of the fertilized ovum arises from the egg-substance precisely

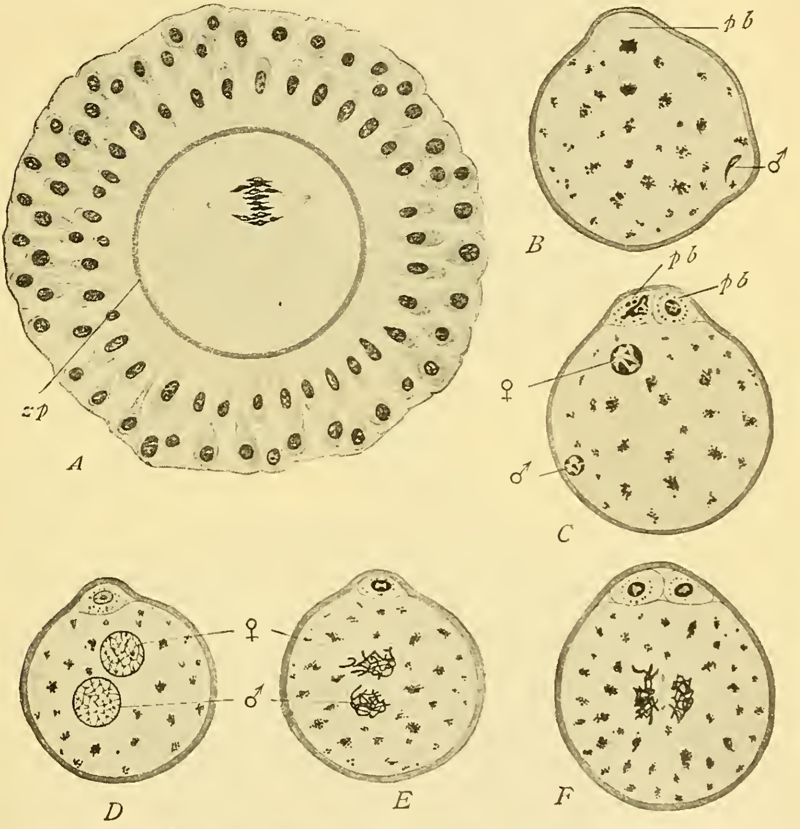

Fig. 92. — Maturation and fertilization of the egg of the mouse. [SOBOTTA.]

A. The ovarian egg still surrounded by the follicle-cells and the membrane (*z.p.* zona pellucida); the polar spindle formed. *B.* Egg immediately after entrance of the spermatozoön (sperm-nucleus at ♂). *C.* The two germ-nuclei (♂, ♀) still unequal; polar bodies above. *D.* Germ-nuclei approaching, of equal size. *E.* The chromosomes forming. *F.* The minute cleavage-spindle in the centre; on either side the paternal and maternal groups of chromosomes.

as in the ordinary mitosis of tissue-cells, and its mode of origin therefore involves the same questions as those already discussed at page 72. It is quite otherwise with the centrosomes at the astral centres, the origin of which still remains one of the most difficult, as it is one of the most interesting, problems relating to fertilization.

After the formation of the polar bodies, the egg-nucleus is reconstituted near the upper pole of the egg, and the entire polar mitotic apparatus disappears. In the meantime a new astral system (sperm-

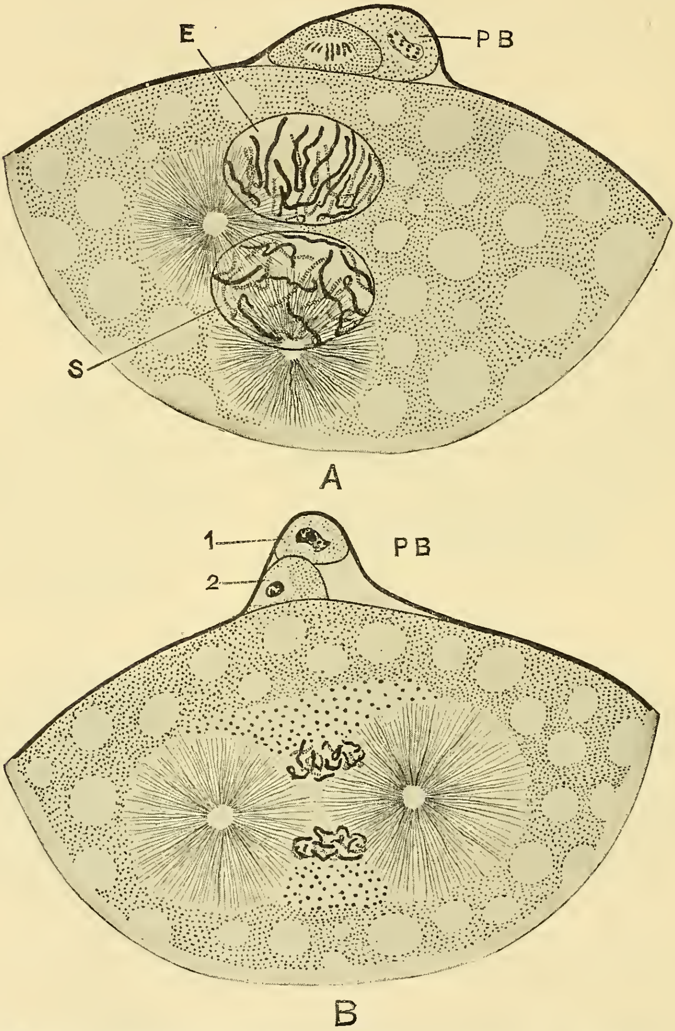

Fig. 93. — Fertilization of the egg of the gasteropod, *Pterotrachea*. [Boveri.]

A. The egg-nucleus (*E*) and sperm-nucleus (*S*) approaching after formation of the polar bodies; the latter shown above (*P. B.*); each germ-nucleus contains sixteen chromosomes; the sperm-amphiaster fully developed. *B.* The mitotic figure for the first cleavage nearly established; the nuclear membranes have disappeared, leaving the maternal group of chromosomes above the spindle, the paternal below it.

aster or amphiaster) is developed in the neighbourhood of the sperm-nucleus, and this in a large number of cases gives rise or is definitely related to the cleavage-amphiaster (cœlenterates, flat-worms, echinoderms, nematodes, annelids, arthropods, mollusks, tunicates, vertebrates). In many of these cases the sperm-aster, which by division gives rise to the amphiaster, has been found to arise in intimate relation with the middle-piece of the spermatozoön; *e.g.* in echinoderms (Flemming, Hertwig, Boveri, Wilson, Mathews, Hill, etc.), in the axolotl (Fick) and salamander (Michælis), in the tunicates (Hill), annelids (Foot, Vejdovsky), insects (Henking), nematodes (Meyer, Erlanger), and mollusks (Henking, Kostanecki, and Wierzejski). The agreement between forms so diverse is very strong evidence that this is a very general phenomenon, and it is one of great interest, owing to the fact that the middle-piece is itself derived from or contains the centrosome of the spermatid.[1]

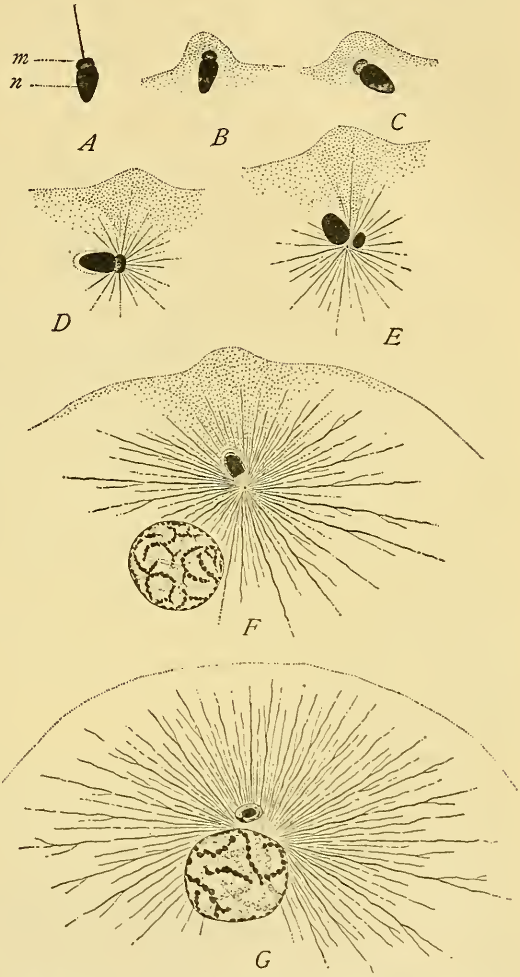

Fig. 94. — Entrance and rotation of the sperm-head and formation of the sperm-aster in the sea-urchin, *Toxopneustes* (*A–F*, × 1600; *G*, *H*, × 800).

A. Sperm-head before entrance; *n*. nucleus; *m*. middle-piece and part of the flagellum. *B*. *C*. Immediately after entrance, showing entrance-cone. *D*. Rotation of the sperm-head, formation of the sperm-aster about the middle-piece. *E*. Casting off of middle-piece; centrosome at focus of the rays (*cf.* Fig. 12). The changes figured occupy about eight minutes. *F*. *G*. Approach of the germ-nuclei; growth of the aster.

The facts may be illustrated by a brief description of the phenomena in the sea-urchin *Toxopneustes* (Fig. 94). As described at page 197, the tail is in this case left outside, and only the head and middle-piece enter the egg. Within a few minutes after its entrance, and while still very near the periphery, the lance-shaped sperm-head, carrying the middle-piece at its base, rotates through nearly or quite 180°, so that the pointed end is directed outward and the middle-piece is turned inward (Fig. 94, *A–F*).[1] During or shortly after the rotation appears a minute aster centring in or very near the middle-piece. As it enlarges, the middle-piece itself is thrown to one side (Fig. 12), where it soon degenerates, while in the centre of the aster a minute intensely staining centrosome may be seen. Both sperm-nucleus and aster now rapidly advance toward the centre of the egg, the aster leading the way and its rays extending far out into the cytoplasm and finally traversing nearly an entire hemisphere. The central mass of the aster comes in contact with the egg-nucleus, divides into two, and the daughter-asters pass to opposite poles of the egg-nucleus, while the sperm-nucleus flattens against the latter and assumes the form of a biconvex lens (Fig. 95). The nuclei now fuse to form the cleavage-nucleus. Shortly afterward the nuclear membrane fades away, a spindle is developed between the asters, and a group of chromosomes arises from the cleavage-nucleus. These are 36 or 38 in number; and although their relation to the paternal and maternal chromatin cannot in this case be accurately traced, owing to the apparent fusion of the nuclei, there can be no doubt on general grounds that one-half have been derived from each germ-nucleus. The egg then divides into two, four, etc., by ordinary mitosis (Figs. 4, 52).

---

[1] *Cf.* p. 170.

In the type of fertilization just described, the polar bodies are formed long before the entrance of the spermatozoön and the germ-nuclei conjugate immediately upon entrance of the spermatozoön, fusing to form a true cleavage-nucleus. In a second and more frequent type (*Ascaris*, Fig. 90; *Physa*, Fig. 89; *Nereis*, Fig. 97; *Cyclops*, Fig. 98) the sperm-nucleus penetrates for a certain distance, often to the centre of the egg, and then pauses while the polar bodies are formed. It then conjugates with the re-formed egg-nucleus. In this case the sperm-aster always divides to form an amphiaster before conjugation of the nuclei, while in the first case the aster may be still undivided at the time of union. This difference is doubtless due merely to a difference in the time elapsing between entrance of the spermatozoön and conjugation of the nuclei, the amphiaster having, in the second case, time to form during extrusion of the polar bodies. The two types just described (Fig. 96) are connected by various gradations. Thus, in the lamprey, the frog, the rabbit, and in *Amphioxus*, one polar body is expelled before, and one after, the entrance of the spermatozoön; in the annelid *Ophryotrocha*, entrance takes place when the first polar spindle is in the stage of the equatorial plate;

---

[1] The first, as far as I know, to observe the rotation of the sperm-head was Flemming in the echinoderm-egg ('81, pp. 17–19). It has since been clearly observed in several other cases, and is probably a phenomenon of very general occurrence.

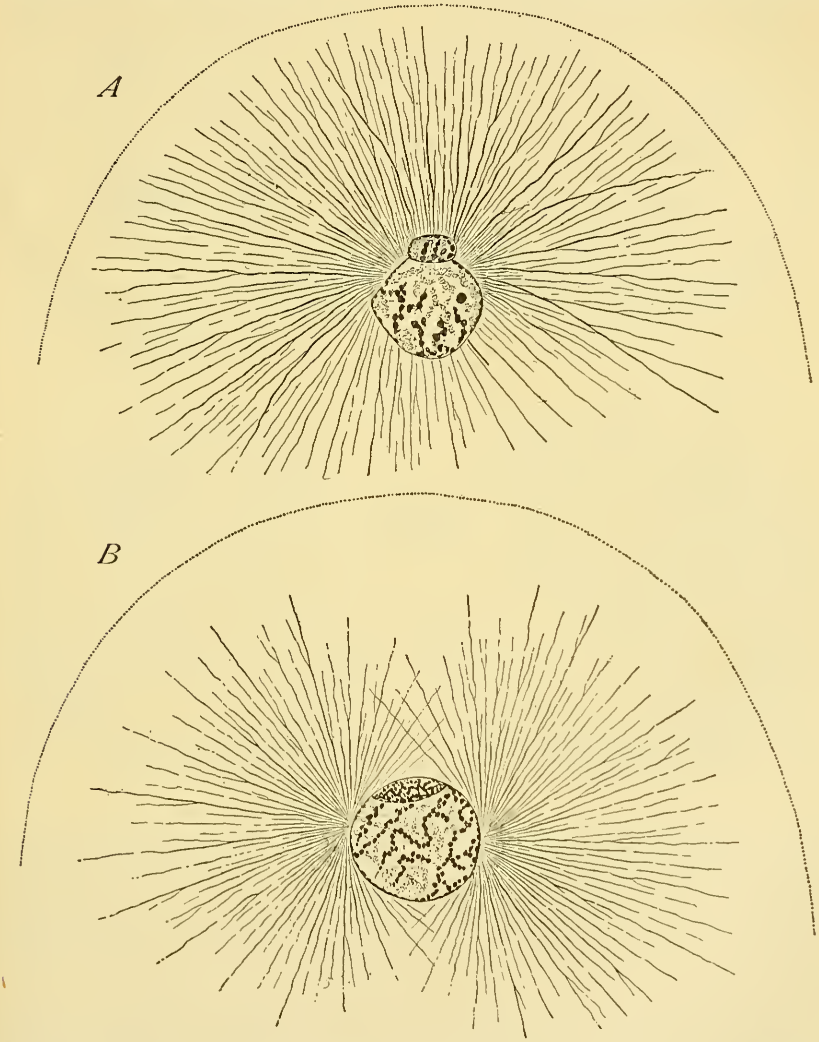

Fig. 95. — Conjugation of the germ-nuclei and division of the sperm-aster in the sea-urchin *Toxopneustes*, × 1000. (For later stages see Fig. 52.)

A. Union of the nuclei; extension of the aster. *B.* Flattening of the sperm-nucleus against the egg-nucleus; division of the aster.

while in *Chætopterus* and *Pieris* the first polar spindle has advanced into the anaphase.[1]

It is an interesting and significant fact that the aster or amphiaster always leads the way in the march toward the egg-nucleus; and in many cases it may be far in advance of the sperm-nucleus.[2] Boveri ('87, 1) has observed in sea-urchins that the sperm-nucleus may indeed be left entirely behind, the aster alone conjugating with the egg-nucleus and causing division of the egg *without union of the germ-nuclei*, though the sperm-nucleus afterward conjugates with one of the nuclei of the two-cell stage. This process, known as "partial fertilization," is undoubtedly to be regarded as abnormal. It affords, however, a beautiful illustration of the view that *it is the centrosome alone that incites division of the egg, and is therefore the fertilizing element proper* (Boveri, '87, 2).

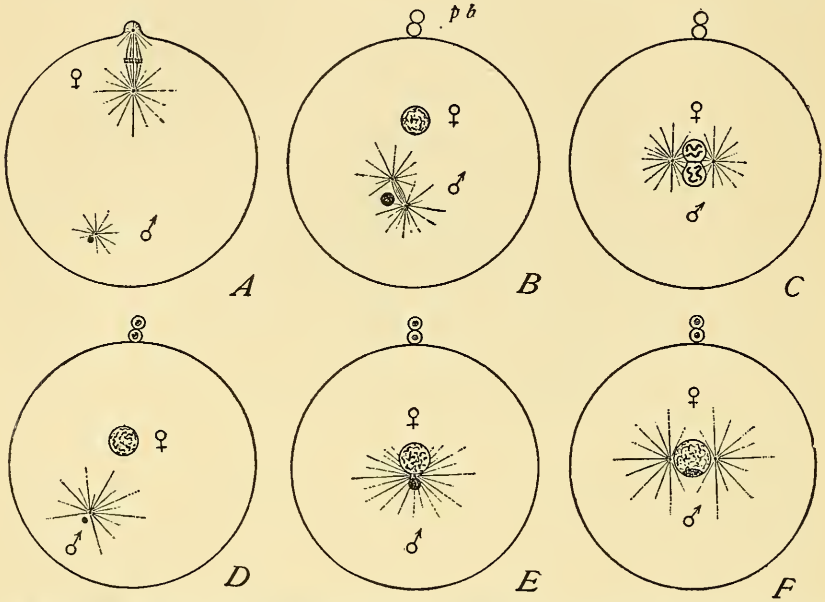

Fig. 96.—Diagrams of two principal types of fertilization. *I.* Polar bodies formed after the entrance of the spermatozoa (annelids, mollusks, flat-worms). *II.* Polar bodies formed before entrance (echinoderms).

A. Sperm-nucleus and centrosome at ♂; first polar body forming at ♀.. *B.* Polar bodies formed; approach of the nuclei. *C.* Union of the nuclei. *D.* Approach of the nuclei. *E.* Union of the nuclei. *F.* Cleavage-nucleus.

The foregoing facts lead us to a consideration of Boveri's theory of fertilization, which has for several years formed a central point of discussion. The ground for this theory had been prepared by Oscar

---

[1] *Cf.* p. 181.

[2] *Cf.* Kostanecki and Wierzejski, '96.

Hertwig and Fol. The latter ('73) early reached the conclusion that the asters represented "centres of attraction" lying outside and independent of the nucleus. Oscar Hertwig showed, in 1875, that in the sea-urchin egg, the amphiaster arises by the division of a single aster that first appears near the sperm-nucleus and accompanies it in its progress toward the egg-nucleus. A similar observation was soon afterward made by Fol ('79) in the eggs of *Asterias* and *Sagitta*, and in the latter case he determined the fact that the astral

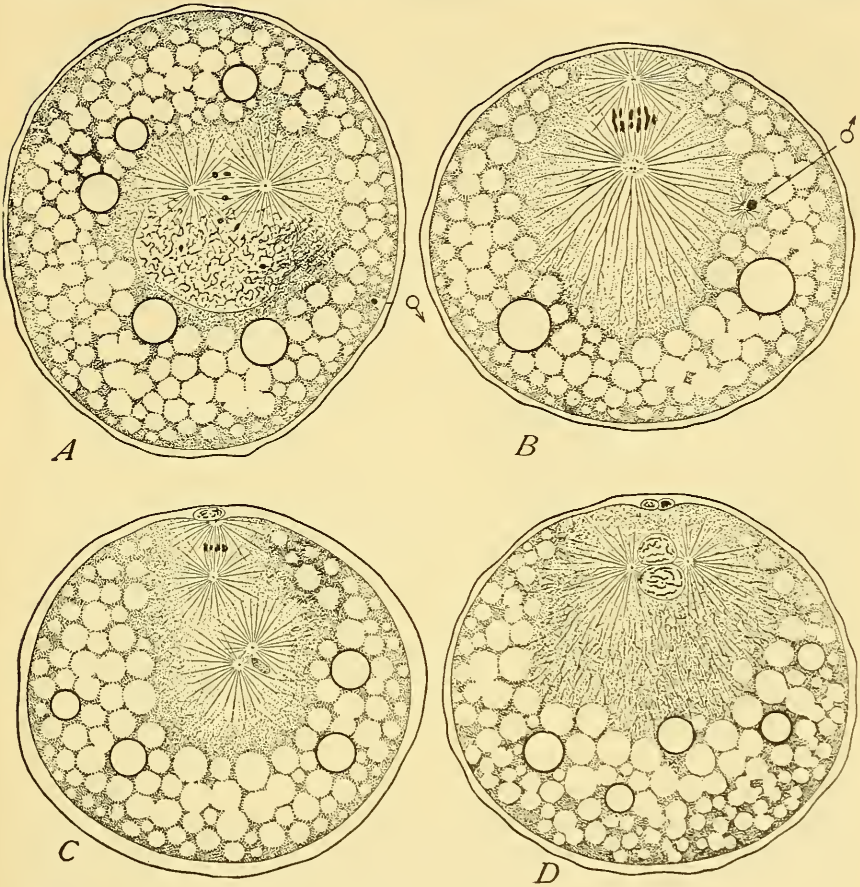

Fig. 97. — Fertilization of the egg of *Nereis*, from sections. (× 400.)

A. Soon after the entrance of the spermatozoön, showing the minute sperm-nucleus at ♂, the germinal vesicle disappearing, and the first polar mitotic figure forming. The empty spaces represent deutoplasm-spheres (slightly swollen by the reagents), the firm circles oil-drops. *B*. Sperm-nucleus (♂) advancing, a minute amphiaster in front of it; first polar mitotic figure established; polar concentration of the protoplasm. *C*. Later stage; second polar body forming. *D*. The polar bodies formed; conjugation of the germ-nuclei; the egg-centrosomes and asters have disappeared, leaving only the sperm-amphiaster (*cf.* Fig. 60).

rays do not centre in the nucleus, as Hertwig described, *but at a point in advance of it* — a fact afterward confirmed by Hertwig himself and by Boveri ('88, 1). Hertwig and Fol afterward found that in cases of polyspermy, when several spermatozoa enter the egg, each sperm-nucleus is accompanied by an aster, and Hertwig proved that each of these might give rise to an amphiaster (Fig. 101). In 1886–87 Vejdovsky brought forward strong evidence to show that in the fresh-water annelid *Rhynchelmis* the cleavage-amphiaster arises directly from the sperm-amphiaster, itself derived by the division of a "periplast" (attraction-sphere) imported into the egg by the spermatozoön, while the polar amphiaster entirely disappears. It was Boveri ('87, 2) who first carefully studied the facts with reference to the centrosome, reaching the conclusion (in the case of *Ascaris* and the sea-urchin) that a single centrosome is brought in by the spermatozoön, and that it divides to form two centres about which are developed the two asters of the cleavage-figure. He was thus led to the following conclusion, which has received the support of many later investigators: *The ripe egg possesses all of the organs and qualities necessary for division excepting the centrosome, by which division is initiated. The spermatozoön, on the other hand, is provided with a centrosome, but lacks the substance in which this organ of division may exert its activity. Through the union of the two cells in fertilization, all of the essential organs necessary for division are brought together; the egg now contains a centrosome which by its own division leads the way in the embryonic development.*[1] Very numerous observations, supporting this conclusion, have been made by later observers. Böhm could find in *Petromyzon* ('88) and the trout ('91) no radiations near the egg-nucleus after the formation of the polar-bodies, while a beautiful sperm-aster is developed near the sperm-nucleus and divides to form the amphiaster. Platner ('86) had already made similar observations in the snail *Arion*, and the same result was soon afterward reached by Brauer ('92) in the case of *Branchipus*, and by Julin ('93) in *Styleopsis*. Fick's careful study of fertilization of the axolotl ('93) proved in a very convincing manner not only that the amphiaster is a product of the sperm-aster, but also that the latter is developed about the *middle-piece* as a centre. The same result was indicated by Foot's observations on the earthworm ('94), and it was soon afterward conclusively demonstrated in echinoderms through the independent and nearly simultaneous researches of myself on the egg of *Toxopneustes*, of Mathews on *Arbacia*, and of Boveri on *Echinus*. Nearly at the same time a careful study was made by Mead ('95, '98, 1) of the annelid *Chætopterus*, and of the starfish *Asterias* by Mathews, both observers independently showing that the polar spindle contains distinct centrosomes, which, however, degenerate after the formation of the polar bodies, their place being taken by the sperm-centrosome, which divides to form an amphiaster before union of the nuclei, as in *Rhynchelmis.* Exactly the same result has since been reached by Hill ('95) and Reinke ('95) in *Sphærechinus*, by Hill in the tunicate *Phallusia*, by Kostanecki and Wierzejski ('96) in *Physa* (Fig. 89), and by Van der Stricht ('98) in *Thysanozoön ;* and in all of these the centrosome is likewise shown to arise from the middle-piece or in its immediate neighbourhood. Among others who have produced evidence that the cleavage-centrosome stands in definite relation to the spermatozoön, may be mentioned Oppel ('92) in reptiles, Brauer ('92) in *Branchipus*, Henking ('92) in insects, Rückert ('95, 2) in *Cyclops*, Sobotta ('95) in the mouse and ('98) *Amphioxus*, Ziegler ('95) in *Diplogaster* and *Rhabditis*, Castle ('96) in *Ciona*, Korschelt ('95) in *Ophryotrocha*, Meyer ('95) in *Strongylus*, Griffin ('96, '99) in *Thalassema*, and Coe ('98) in *Cerebratulus*.

---

[1] '87, 2, p. 155.

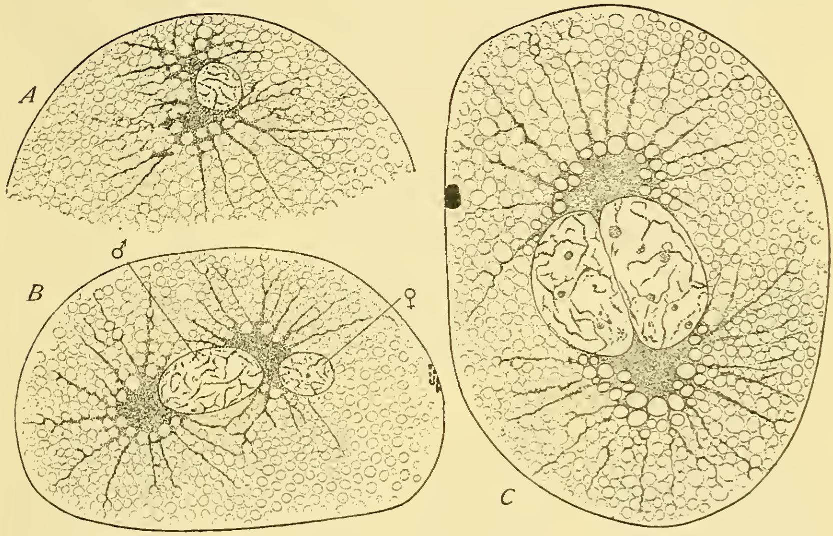

Fig. 98. — Fertilization of the egg in the copepod, *Cyclops strenuus*. [RÜCKERT.]

A. Sperm-nucleus soon after entrance, the sperm-aster dividing. *B*. The germ-nuclei approaching; ♂, the enlarged sperm-nucleus with a large aster at each pole; ♀, the egg-nucleus re-formed after formation of the second polar body, shown at the right. *C*. The apposed reticular germ-nuclei, now of equal size; the spindle is immediately afterward developed between the two enormous sperm-asters; polar body at the left.

Beside the foregoing evidence may be placed the following additional data based on experiment and the study of pathological fertilization. (1) In the case of sea-urchin eggs, Hertwig, Boveri, and several later observers have shown that egg-fragments, obtained by shaking eggs to pieces, are readily penetrated by the spermatozoa, and that such fragments, though containing no nuclear matter from the egg, may segment and give rise to perfect larvæ.[1] (2) Boveri ('88) has observed that in ordinary fertilization the sperm-aster may separate from the sperm-nucleus, travel through the cytoplasm to the egg-nucleus and cause cleavage, the sperm-nucleus afterward fusing with one of the nuclei of the two-cell stage ("partial fertilization"). (3) Most remarkable of all, Boveri, confirmed by Ziegler ('98), has recently observed that during the first cleavage the whole of the chromatin may pass to one pole, so that upon division one of the halves of the egg receives only a centrosome without a nucleus. In the nucleated half cleavage proceeds as usual. In the enucleated half the centrosomes and asters continue for a considerable period to multiply at the same rate as the cleavage of the nucleated half, though the cell-body does not itself divide.[2] Putting these facts together we must conclude (1) that something is introduced into the egg by the middle-piece of each spermatozoön entering it that is either a centrosome or has the power to incite the formation of one; (2) that the centrosome thus arising is structurally independent of both nuclei and may divide independently of them; (3) that independently of the division of the nucleus or cell-body there is some kind of historical continuity between the centrosomes of successive generations.

In the case of echinoderm-eggs this continuity is not yet known to be effected by actual persistence of the centrosomes.[3] There are, however, a number of cases in which the division of the primary cleavage-centrosomes and the persistence of their descendants as those of the daughter-cells seem to have been conclusively shown — for example on *Ascaris* (Van Beneden, Boveri, Kostanecki, and Siedlecki), in the trout (Henneguy, '96), in *Thalassema* (Griffin, '96, '99), in *Chætopterus* (Mead, '95, '98), in *Physa* (Kostanecki and Wierzejski, '96), in *Cerebratulus* (Coe, '98), and in *Rhynchelmis* (Vejdovsky and Mrazek, '98). In *Thalassema* and *Cerebratulus* (Figs. 99, 155) the centrosome is a minute granule at the focus of the sperm-aster, which divides to form an amphiaster soon after the entrance of the spermatozoön. During the early anaphase of the first cleavage, each centrosome divides into two, passes to the outer periphery of the centrosphere, and there forms a minute amphiaster for the second cleavage before the first cleavage takes place. The minute centrosomes of the second cleavage are therefore the direct descendants of the sperm-centrosome; and there is good reason to believe that the continuity is not broken in later stages. The facts are nearly similar in the trout, in *Chætopterus*, and in *Physa*. In *Ascaris* division of the centrosome first occurs at a somewhat later period (Figs. 90, 176). If now the centrosomes were indeed permanent cell-organs, we should thus reach the following result: *During cleavage the cytoplasm of the blastomeres is derived from that of the egg, the centrosomes from*

---

[1] *Cf.* p. 353.

[2] *Cf.* p. 108.

[3] Erlanger's statement ('98) that the centrosomes persist through the first cleavage in echinoderm-eggs is not supported by his figures; and I am convinced from my own long-continued studies of these eggs, as well as by an examination of Erlanger's preparations, kindly placed in my hands by Professor Bütschli, that these difficult objects are very unfavourable for a decision of the question.

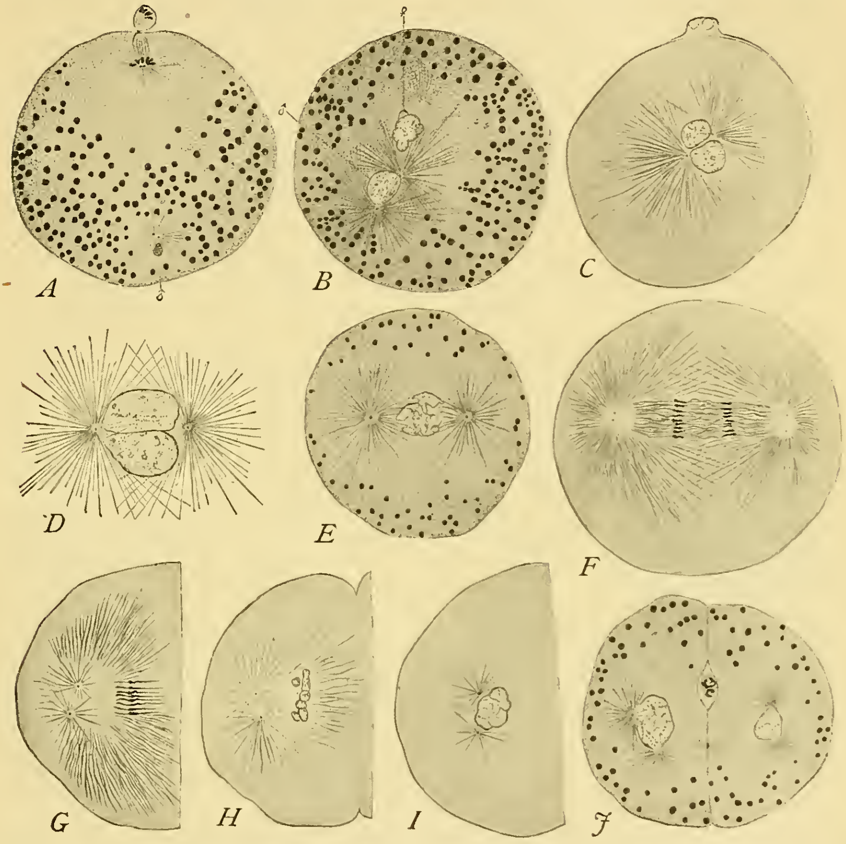

Fig. 99. — Fertilization in an annelid (armed Gephyrean), *Thalassema*. [GRIFFIN.]

A. Second polar body forming; sperm-nucleus and centrosome below. *B.* Approach of the egg-nucleus and sperm-nucleus, the latter accompanied by the sperm-amphiaster. *C.* Union of the nuclei. *D.* Later stage of last. *E.* Prophase of cleavage-spindle. *F.* Anaphase of the same; centrosome divided. *G. H. I.* Successive stages in the nuclear reconstitution and formation of the daughter-amphiasters for the second cleavage. *J.* Two-cell stage.

the spermatozoön, while the nuclei (*chromatin*) *are equally derived from both germ-cells.*

There is very strong reason to accept the first part of this conclusion (applying to nucleus and cytoplasm), but the question of the centrosomes remains an open one. The array of evidence given above, derived from the study of so many diverse groups, seems to place Boveri's lucid and enticing hypothesis upon a strong foundation. Two essential points still remain, however, to be determined: first, whether the facts observed in *Ascaris*, Echinoderms, *Physa*, *Thalassema*, and the like, are typical of all forms of fertilization; and, second, whether, if so, the primary cleavage-centrosome is actually imported into the egg by the spermatozoön or is only formed under its influence out of the egg-substance. Both these questions have been raised by recent investigators, apparently on good evidence, and some of this evidence is directly opposed to both of the principal assumptions of Boveri's theory. Thus, Wheeler ('97) has found that in *Myzostoma* both centrosomes are derived from the egg; Carnoy and Le Brun ('97) maintain that in *Ascaris* one centrosome is derived from each of the germ-nuclei; in some mollusks, according to MacFarland ('97) and Lillie ('97), both egg-centrosomes and sperm-centrosomes disappear, to be replaced by two centrosomes of unknown origin; while recent botanical workers are unable to find any centrosomes in fertilization. These and other divergent results will be critically considered beyond (p. 208) in connection with a more detailed examination of the general subject. It may be pointed out here, however, that recent researches on spermatogenesis (p. 170) render it nearly certain that the centrosome of the sperm-aster cannot be the unmodified centrosome of the spermatid, since the latter, in some cases, enlarges to form a "middle-piece" or analogous structure that is far larger than the sperm-centrosome.

B. UNION OF THE GERM-CELLS

It does not lie within the scope of this work to consider the innumerable modes by which the germ-cells are brought together, further than to recall the fact that their union may take place inside the body of the mother or outside, and that in the latter case both eggs and spermatozoa are as a rule discharged into the water, where fertilization and development take place. The spermatozoa may live for a long period, either before or after their discharge, without losing their fertilizing power, and their movements may continue throughout this period. In many cases they are motionless when first discharged, and only begin their characteristic swimming movements after coming in contact with the water. There is clear evidence of a definite attraction between the germ-cells, which is in some cases so marked (for example in the polyp *Renilla*) that when spermatozoa and ova are mixed in a small vessel, each ovum becomes in a few moments surrounded by a dense fringe of spermatozoa attached to its periphery by their heads and by their movements actually causing the ovum to move about. The nature of the attraction is not positively known, but Pfeffer's researches on the spermatozoids of plants leave little doubt that it is of a chemical nature, since he found the spermatozoids of ferns and of *Selaginella* to be as actively attracted by solutions of malic acid or malates (contained in capillary tubes) as by the substance extruded from the neck of the archegonium. Those of mosses, on the other hand, are indifferent to malic acid, but are attracted by cane-sugar. These experiments indicate that the specific attraction between the germ-cells of the same species is owing to the presence of specific chemical substances in each case. There is clear evidence, furthermore, that the attractive force is not exerted by the egg-nucleus alone, but by the egg-cytoplasm; for, as the Hertwigs and others have shown, spermatozoa will readily enter egg-fragments entirely devoid of a nucleus.

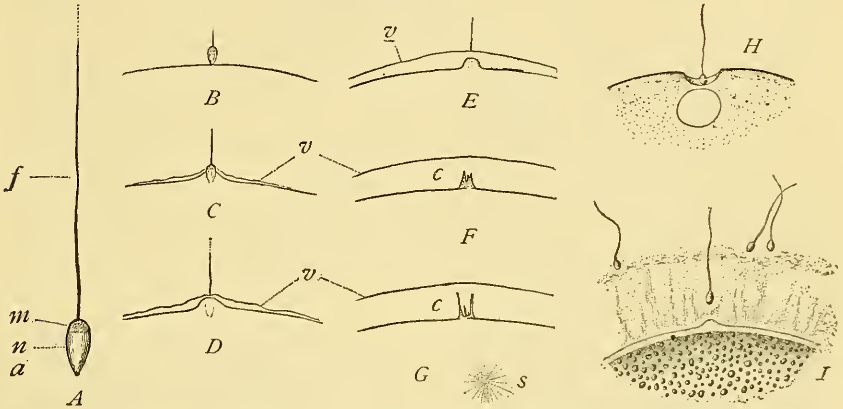

Fig. 100. — Entrance of the spermatozoön into the egg. *A–G.* In the sea-urchin, *Toxopneustes. H.* In the medusa, *Mitrocoma.* [METSCHNIKOFF.] *I.* In the star-fish *Asterias.* [FOL.]

A. Spermatozoön of *Toxopneustes*, × 2000; *a.* the apical body, *n.* nucleus, *m.* middle-piece, *f.* flagellum. *B.* Contact with the egg-periphery. *C. D.* Entrance of the head, formation of the entrance-cone and of the vitelline membrane (*v*), leaving the tail outside. *E. F.* Later stages. *G.* Appearance of the sperm-aster (*s*) about 3–5 minutes after first contact; entrance-cone breaking up. *H.* Entrance of the spermatozoön into a preformed depression. *I.* Approach of the spermatozoön, showing the preformed attraction-cone.

In naked eggs, such as those of some echinoderms, and cœlenterates, the spermatozoön may enter at any point; but there are some cases in which the point of entrance is predetermined by the presence of special structures through which the spermatozoön enters (Fig. 100). Thus, the starfish-egg, according to Fol, possesses before fertilization a peculiar protoplasmic "attraction-cone" to which the head of the spermatozoön becomes attached, and through which it enters the egg. In some of the hydromedusæ, on the other hand, the entrance point is marked by a funnel-shaped depression at the egg-periphery (Metschnikoff). When no preformed attraction-cone is present, an "entrance-cone" is sometimes formed by a rush of protoplasm toward the point at which the spermatozoön strikes the egg and there forming a conical elevation into which the sperm-head passes. In the sea-urchin (Fig. 100) this structure persists only a short time after the spermatozoön enters, soon assuming a ragged flame-shape and breaking up into slender rays. In some cases the egg remains naked, even after fertilization, as appears to be the case in many cœlenterates. More commonly a vitelline membrane is quickly formed after contact of the spermatozoön, — *e.g.* in *Amphioxus*, in the echinoderms, and in many plants, — and by means of this the entrance of other spermatozoa is prevented. In eggs surrounded by a membrane before fertilization, the spermatozoön either bores its way through the membrane at any point, as is probably the case with mammals and Amphibia, or may make its entrance through a micropyle.

In some forms only one spermatozoön normally enters the ovum, as in echinoderms, mammals, many annelids, etc., while in others several may enter (insects, elasmobranchs, reptiles, the earthworm, *Petromyzon*, etc.). In the former case more than one spermatozoön may accidentally enter (pathological polyspermy), but development is then always abnormal. In such cases each sperm-centrosome gives rise to an amphiaster, and the asters may then unite to form the most complex polyasters, the nodes of which are formed by the centrosomes (Fig. 101). Such eggs either do not divide at all or undergo an irregular multiple cleavage and soon perish. If, however, only two spermatozoa enter, the egg may develop for a time. Thus Driesch has determined the interesting fact, which I have confirmed, that sea-urchin eggs into which two spermatozoa have accidentally entered undergo a double cleavage, dividing into four at the first cleavage, and forming eight instead of four micromeres at the fourth cleavage. Such embryos develop as far as the blastula stage, but never form a gastrula.[1] In cases where several spermatozoa normally enter the egg (physiological polyspermy), only one of the sperm-nuclei normally unites with the egg-nucleus, the supernumerary sperm-nuclei either degenerating, or in rare cases — *e.g.* in elasmobranchs and reptiles — living for a time and even dividing to form

---

[1] For an account of the internal changes, see p. 355.

"merocytes" or accessory nuclei. The fate of the latter is still in doubt; but they certainly take no part in fertilization.

It is an interesting question how the entrance of supernumerary spermatozoa is prevented in normal monospermic fertilization. In the case of echinoderm-eggs Fol advanced the view that this is mechanically effected by means of the vitelline membrane formed instantly after the first spermatozoön touches the egg. This is indicated by the following facts. Immature eggs, before the formation of the polar bodies, have no power to form a vitelline membrane, and the spermatozoa always enter them in considerable numbers. Polyspermy also takes place, as O. and R. Hertwig's beautiful experiments showed ('87), in ripe eggs whose vitality has been diminished by the action of dilute poisons, such as nicotine, strychnine, and morphine, or by subjection to an abnormally high temperature

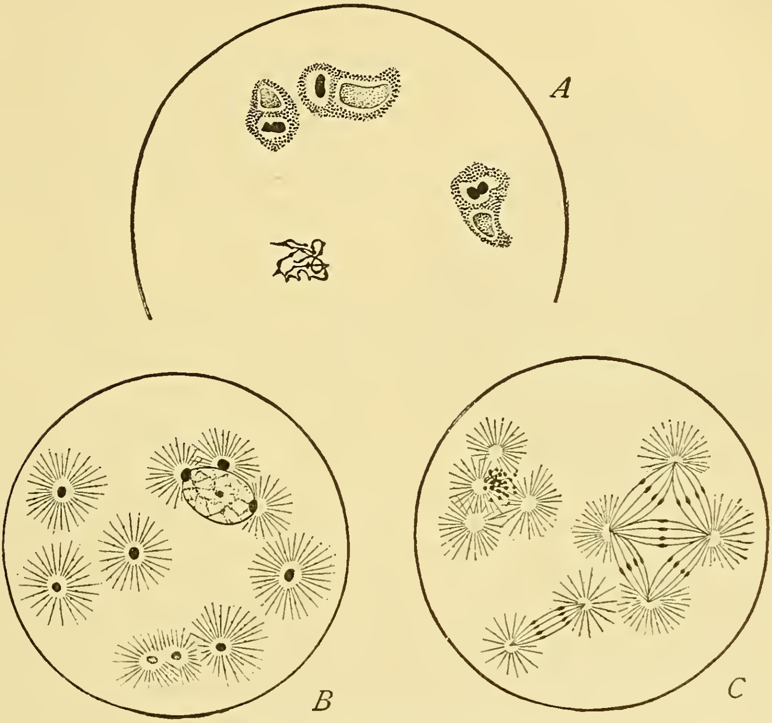

Fig. 101.— Pathological polyspermy.

A. Polyspermy in the egg of *Ascaris*; below, the egg-nucleus; above, three entire spermatozoa within the egg. [SALA.]

B. Polyspermy in sea-urchin egg treated with 0.005% nicotine solution; ten sperm-nuclei shown, three of which have conjugated with the egg-nucleus. *C.* Later stage of an egg similarly treated, showing polyasters formed by union of the sperm-amphiasters. [O. and R. HERTWIG.]

(31° C.); and in these cases the vitelline membrane is only slowly formed, so that several spermatozoa have time to enter.[1] Similar mechanical explanations have been given in various other cases. Thus Hoffman believes that in teleosts the micropyle is blocked by the polar bodies after the entrance of the first spermatozoön; and Calberla suggested (*Petromyzon*) that the same result might be caused by the tail of the entering spermatozoön. It is, however, far from certain whether such rude mechanical explanations are adequate; and there is considerable reason to believe that the egg may possess a physiological power of exclusion called forth by the first spermatozoön. Thus Driesch found that spermatozoa did not enter fertilized sea-urchin eggs from which the membranes had been removed by shaking.[2] In some cases no membrane is formed (some cœlenterates), in others several spermatozoa are found inside the membrane (nemertines), in others the spermatozoön may penetrate the membrane at any point (mammals), yet monospermy is the rule.

1. *Immediate Results of Union*

The union of the germ-cells calls forth profound changes in both.

(*a*) *The Spermatozoön.* — Almost immediately after contact the tail ceases its movements. In some cases the tail is left outside, being carried away on the outer side of the vitelline membrane, and only the head and middle-piece enter the egg (echinoderms, Fig. 100). In other cases the entire spermatozoön enters (amphibia, earthworm, insects, etc., Fig. 89), but the tail always degenerates within the ovum and takes no part in fertilization. Within the ovum the sperm-nucleus rapidly grows, and both its structure and staining-capacity rapidly change (*cf.* p. 182). The most important and significant result, however, is *an immediate resumption by the sperm-nucleus and sperm-centrosome of the power of division*, which has hitherto been suspended. This is not due to the union of the germ-nuclei; for, as the Hertwigs and others have shown, the supernumerary sperm-nuclei in polyspermic eggs may divide freely without copulation with the egg-nucleus, and they divide as freely after entering enucleated egg-fragments. The stimulus to division must therefore be given by the egg-cytoplasm. It is a very interesting fact that in some cases the cytoplasm has this effect on the sperm-nucleus

---

[1] The Hertwigs attribute this to a diminished irritability on the part of the egg-substance. Normally requiring the stimulus of only a single spermatozoön for the formation of the vitelline membrane, it here demands the more intense stimulus of two, three, or more before the membrane is formed. That the membrane is not present before fertilization is admitted by Hertwig on the ground stated at page 132.

[2] On the other hand, Morgan states ('95, 5, p. 270) that one or more spermatozoa will enter nucleated or enucleated egg-fragments whether obtained before or after fertilization.

only after formation of the polar bodies; for when in sea-urchins the spermatozoa enter immature eggs, as they freely do, they penetrate but a short distance, and no further change occurs.

(*b*) *The Ovum.* — The entrance of the spermatozoön produces an extraordinary effect on the egg, which extends to every part of its organization. The rapid formation of the vitelline membrane, already described, proves that the stimulus extends almost instantly throughout the whole ovum.[1] At the same time the physical consistency of the cytoplasm may greatly alter, as for instance in echinoderm eggs, where, as Morgan has observed, the cytoplasm assumes immediately after fertilization a peculiar viscid character which it afterward loses. In many cases the egg contracts, performs amœboid movements, or shows wave-like changes of form. Again, the egg-cytoplasm may show active streaming movements, as in the formation of the entrance-cone in echinoderms, or in the flow of peripheral protoplasm toward the region of entrance to form the germinal disc, as in many pelagic fish-eggs. An interesting phenomenon is the formation, behind the advancing sperm-nucleus, of a peculiar funnel-shaped mass of deeply staining material extending outward to the periphery. This has been carefully described by Foot ('94) in the earthworm, where it is very large and conspicuous, and I have since observed it also in the sea-urchin (Fig. 94).

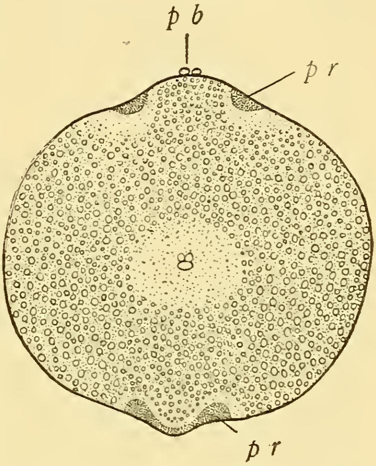

Fig. 102. — Egg of the leech *Clepsine* during fertilization. [Whitman.]

p.b. polar bodies; *p.r.* polar rings; cleavage-nucleus near the centre.

The most profound change in the ovum is, however, the migration of the germinal vesicle to the periphery and the formation of the polar bodies. In many cases either or both these processes may occur before contact with the spermatozoön (echinoderms, some vertebrates). In others, however, the egg awaits the entrance of the spermatozoön (annelids, gasteropods, etc.), which gives it the necessary stimulus. This is well illustrated by the egg of *Nereis*. In the newly discharged egg the germinal vesicle occupies a central position, the yolk, consisting of deutoplasm-spheres and oil-globules, is uniformly distributed, and at the periphery of the egg is a zone of clear perivitelline protoplasm (Fig. 60). Soon after entrance of the spermatozoön the germinal vesicle moves toward the periphery, its membrane fades away, and a radially directed mitotic figure appears, by means of which the first polar body is formed (Fig. 97). Meanwhile the protoplasm flows toward the upper pole, the peri-vitelline zone disappears, and the egg now shows a sharply marked polar differentiation. A remarkable phenomenon, described by Whitman in the leech ('78), and later by Foot in the earthworm ('94), is the formation of "polar rings," a process which follows the entrance of the spermatozoön and accompanies the formation of the polar bodies. These are two ring-shaped cytoplasmic masses which form at the periphery of the egg near either pole and advance thence toward the poles, the upper one surrounding the point at which the polar bodies are formed (Fig. 102). Their meaning is unknown, but Foot ('96) has made the interesting discovery that they are probably of the same nature as the yolk-nuclei (p. 156).

---

[1] I have often observed that the formation of the membrane, in *Toxopneustes*, proceeds like a wave from the entrance-point around the periphery, but this is often irregular.

2. *Paths of the Germ-nuclei* (*Pro-nuclei*)[1]

After the entrance of the spermatozoön, both germ-nuclei move through the egg-cytoplasm and finally meet one another. The paths traversed by them vary widely in different forms. In general two classes are to be distinguished, according as the polar bodies are formed before or after entrance of the spermatozoön. In the former case (echinoderms) the germ-nuclei unite at once. In the latter case the sperm-nucleus advances a certain distance into the egg and then pauses while the germinal vesicle moves toward the periphery, and gives rise to the polar bodies (*Ascaris*, annelids, etc.). This significant fact proves that the attractive force between the two nuclei is only exerted after the formation of the polar bodies, and hence that the entrance-path of the sperm-nucleus is not determined by such attraction. A second important point, first pointed out by Roux, is that the path of the sperm-nucleus is *curved*, its "entrance-path" into the egg forming a considerable angle, with its "copulation-path" toward the egg-nucleus.

These facts are well illustrated in the sea-urchin egg (Fig. 103), where the egg-nucleus occupies an eccentric position near the point at which the polar bodies are formed (before fertilization). Entering the egg at any point, the sperm-nucleus first moves rapidly inward along an entrance-path that shows no constant relation to the position of the egg-nucleus and is approximately but never exactly radial, *i.e.* toward a point near the centre of the egg. After penetrating a certain distance its direction changes slightly to that of the copulation-path, which, again, is directed not precisely toward the egg-nucleus, but toward a meeting-point where it comes in contact with the egg-nucleus. The latter does not begin to move until the

---

[1] The terms *female pro-nucleus*, *male pro-nucleus* (Van Beneden), are often applied to the germ-nuclei before their union. These should, I think, be rejected in favour of Hertwig's terms *egg-nucleus* and *sperm-nucleus*, on two grounds: (1) The germ-nuclei are true nuclei in every sense, differing from the somatic nuclei only in the reduced number of chromosomes. As the latter character has recently been shown to be true also of the somatic nuclei in the sexual generation of plants (p. 275), it cannot be made the ground for a special designation of the germ-nuclei. (2) The germ-nuclei are not male and female in any proper sense (p. 243).

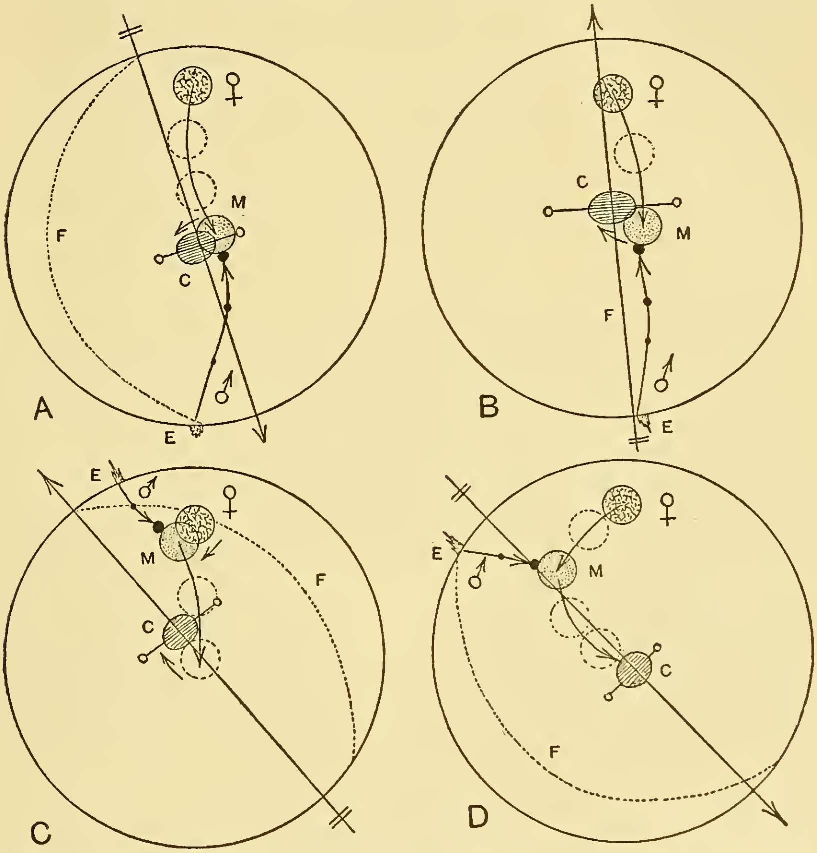

Fig. 103. — Diagrams showing the paths of the germ-nuclei in four different eggs of the sea-urchin, *Toxopneustes*. From camera drawings of the transparent living eggs.

In all the figures the original position of the egg-nucleus (reticulated) is shown at ♀; the point at which the spermatozoön enters at *E* (entrance-cone). Arrows indicate the paths traversed by the nuclei. At the meeting-point (*M*) the egg-nucleus is dotted. The cleavage-nucleus in its final position is ruled in parallel lines, and through it is drawn the axis of the resulting cleavage-figure. The axis of the egg is indicated by an arrow, the point of which is turned away from the micromere-pole. Plane of first cleavage, passing near the entrance-point, shown by the curved dotted line.

entrance-path of the sperm-nucleus changes to the copulation-path. It then begins to move slowly in a somewhat curved path toward the meeting-point, often showing slight amœboid changes of form as it forces its way through the cytoplasm. From the meeting-point the apposed nuclei move slowly toward the point of final fusion, which in this case is near, but never precisely at, the centre of the egg.

These facts indicate that the paths of the germ-nuclei are determined by at least two different factors, one of which is an attraction or other dynamical relation between the nuclei and the cytoplasm, the other an attraction between the nuclei. The former determines the entrance-path of the sperm-nucleus, while both factors probably operate in the determination of the copulation-path along which it travels to meet the egg-nucleus. The real nature of neither factor is known.

Hertwig first called attention to the fact — which is easy to observe in the living sea-urchin egg — that the egg-nucleus does not begin to move until the sperm-nucleus has penetrated some distance into the egg and the sperm-aster has attained a considerable size; and Conklin ('94) has suggested that the nuclei are passively drawn together by the formation, attachment, and contraction of the astral rays. While this view has some facts in its favour, it is, I believe, untenable, for many reasons, among which may be mentioned the fact that neither the actual paths of the pro-nuclei nor the arrangement of the rays support the hypothesis; nor does it account for the conjugation of nuclei when no astral rays are developed (as in Protozoa or in plants). I have often observed in cases of dispermy in the sea-urchin, that both sperm-nuclei move at an equal pace toward the egg-nucleus; but if one of them meets the egg-nucleus first, the movement of the other is immediately retarded, and only conjugates with the egg-nucleus, if at all, after a considerable interval; and in polyspermy the egg-nucleus rarely conjugates with more than two sperm-nuclei. Probably, therefore, the nuclei are drawn together by an actual attraction which is neutralized by union, and their movements are not improbably of a chemotactic character. Conklin ('99) has recently suggested that the nuclei are drawn together by the agency of protoplasmic currents in the egg-substance.

3. *Union of the Germ-nuclei. The Chromosomes*

The earlier observers of fertilization, such as Auerbach, Strasburger, and Hertwig, described the germ-nuclei as undergoing a complete fusion to form the first embryonic nucleus, termed by Hertwig the *cleavage-* or *segmentation-nucleus*. As early as 1881, however, Mark clearly showed that in the slug *Limax* this is not the case, the two nuclei merely becoming apposed without actual fusion. Two years later appeared Van Beneden's epoch-making work on *Ascaris*, in which it was shown not only that the nuclei do not fuse, but that they give rise to two independent groups of chromosomes which separately enter the equatorial plate and whose descendants pass separately into the daughter-nuclei. Later observations have given the strongest reason to believe that, as far as the chromatin is concerned, a true fusion of the nuclei never takes place during fertilization, and that the paternal and maternal chromatin *may* remain separate and distinct in the later stages of development — possibly throughout life (p. 299). In this regard two general classes may be distinguished. In one, exemplified by some echinoderms, by *Amphioxus*, *Phallusia*, and some other animals, the two nuclei meet each other when in the reticular form, and apparently fuse in such a manner that the chromatin of the resulting nucleus shows no visible distinction between the paternal and maternal moieties. In the other class, which includes most accurately known cases, and is typically represented by *Ascaris* (Fig. 90) and other nematodes, by *Cyclops* (Fig. 98), and by *Pterotrachea* (Fig. 93), the two nuclei do not fuse, but only place themselves side by side, and in this position give rise each to its own group of chromosomes. On general grounds we may confidently maintain that the distinction between the two classes is only apparent, and probably is due to corresponding differences in the rate of development of the nuclei, or in the time that elapses before their union.[1] If this time be very short, as in echinoderms, the nuclei unite before the chromosomes are formed. If it be more prolonged, as in *Ascaris*, the chromosome-formation takes place before union.

With a few exceptions, which are of such a character as not to militate against the rule, *the number of chromosomes arising from the germ-nuclei is always the same in both, and is one-half the number characteristic of the tissue-cells of the species. By their union, therefore, the germ-nuclei give rise to an equatorial plate containing the typical number of chromosomes.* This remarkable discovery was first made by Van Beneden in the case of *Ascaris*, where the number of chromosomes derived from each sex is either one or two. It has since been extended to a very large number of animals and plants, a partial list of which follows.

---

[1] Indeed, Boveri has found that in *Ascaris* both modes occur, though the fusion of the germ-nuclei is exceptional. (*Cf.* p. 296.)

A PARTIAL LIST SHOWING THE NUMBER OF CHROMOSOMES CHARACTERISTIC OF THE GERM–NUCLEI AND SOMATIC NUCLEI IN VARIOUS PLANTS AND ANIMALS[1]

GERM-NUCLEI.	SOMATIC NUCLEI.	NAME.	GROUP.	AUTHORITY.
1	2	Ascaris megalocephala, var. univalens.	Nematodes.	Van Beneden, Boveri.
2	4	Id., var. bivalens.	"	"
"	"	Ophryotrocha.	Annelids.	Korschelt.
"	["]	Styleopsis.	Tunicates.	Julin.
4	8	Coronilla.	Nematodes.	Carnoy.
"	"	Pallavicinia.	Hepaticæ.	Farmer.
"	"	Anthoceras.	"	Davis.
6	12	Spiroptera.	Nematodes.	Carnoy.
"	"	Prostheceræus.	Polyclades.	Klinckoström, Francotte.
"	"	Nais.	Phanerogams.	Guignard.
["]	"	Spirogyra.	Conjugatæ.	Strasburger.
"	["]	Gryllotalpa.	Insects.	Vom Rath.
"	"	Caloptenus.	"	Wilcox.
["]	"	Æquorea.	Hydromedusæ.	Häcker.
7	14	Pentatoma.	Insects.	Montgomery.
8	16	Filaroides.	Nematodes.	Carnoy.
"	["]	Prosthiostomum.	Polyclades.	Francotte.
"	["]	Leptoplana.	"	"
"	["]	Cycloporus.	"	"
"	"	Hydrophilus.	Insects.	Vom Rath.
"	"	Phallusia.	Tunicates.	Hill.
"	"	Limax.	Gasteropods.	Vom Rath.
"	["]	Rat.	Mammals.	Moore.
"	["]	Ox, guinea-pig, man.	"	Bardeleben.
"	"	Ceratozamia.	Cyads.	Overton, Guignard.
"	"	Pinus.	Coniferæ.	Dixon.
"	"	Scilla, Triticum.	Angiosperms.	Overton.
"	"	Allium.	"	Strasburger, Guignard.
"	"	Podophyllum.	"	Mottier.
9	18	Echinus.	Echinoderms.	Boveri.
"	"	Thysanozoön.	Polyclades.	Van der Stricht.
"	"	Sagitta.	Chætognaths.	Boveri.
"	"	Chætopterus.	Annelids.	Mead.
"	"	Ascidia.	Tunicates.	Boveri.
10	20	Lasius.	Insects.	Henking.
11	[22]	Allolobophora.	Annelids.	Foot.
12	24	Myzostoma.	"	Wheeler.

---

[1] This table is compiled from papers both on fertilization and maturation. Numbers in brackets are inferred.

GERM-NUCLEI.	SOMATIC NUCLEI.	NAME.	GROUP.	AUTHORITY.
12	24	Thalassema.	Annelids.	Griffin.
11 (12)	22 (24)	Cyclops strenuus.	Copepods.	Rückert.
12	24	„ brevicornis.	„	Häcker.
„	„	Helix.	Gasteropods.	Platner, Vom Rath.
„	„	Branchipus.	Crustacea.	Brauer.
„	„	Pyrrhocoris.	Insects.	Henking.
„	„	Salmo.	Teleosts.	Böhm.
„	„	Salamandra.	Amphibia.	Flemming.
„	„	Rana.	„	Vom Rath.
„	„	Mouse.	Mammals.	Sobotta.
„	„	Osmunda.	Ferns.	Strasburger.
„	„	Lilium.	Angiosperms.	Strasburger. Guignard.
„	„	Helleborus.	„	Strasburger.
„	„	Leucojum, Pæonia, Aconitum.	„	Overton.
14	28	Tiara.	Hydromedusæ.	Boveri.
„	„	Pieris.	Insects.	Henking.
16	32	Cerebratulus, Micrura.	Nemertines.	Coe.
„	„	Pterotrachea, Carinaria, Phyllirhoë.	Gastropods.	Boveri.
„	[„]	Diaptomus, Heterocope.	Copepods.	Rückert.
„	[„]	Anomalocera, Euchæta.	„	Vom Rath.
„	[„]	Lumbricus.	Annelids.	Calkins.
18	36	Torpedo, Pristiurus.	Elasmobranchs.	Rückert.
[18(19)]	36(38)	Toxopneustes.	Echinoderms.	Wilson.
30	[60]	Crepidula.	Gasteropods.	Conklin.
84	168	Artemia.	Crustacea.	Brauer.

The above data are drawn from sources so diverse and show so remarkable a uniformity as to establish the general law with a very high degree of probability. The few known exceptions are almost certainly apparent only and are due to the occurrence of plurivalent chromosomes. This is certainly the case with *Ascaris* (*cf.* p. 87). It is probably the case with the gasteropod *Arion*, where, as described by Platner, the egg-nucleus gives rise to numerous chromosomes, the sperm-nucleus to two only; the latter are, however, plurivalent, for Garnault showed that they break up into smaller chromatin-bodies, and that the germ-nuclei are exactly alike at the time of union. We may here briefly refer to remarkable recent observations by Rückert and others, which seem to show that not only the paternal and maternal chromatin, but also the chromosomes, may retain their individuality throughout development.[1] Van Beneden, the pioneer observer in this direction, was unable to follow the paternal and maternal chromatin beyond the first cleavage-nucleus, though he surmised that they remained distinct in later stages as well; but Rabl and Boveri brought forward evidence that the chromosomes did not lose their identity, even in the resting nucleus. Rückert ('95, 3) and Häcker ('95, 1) have recently shown that in *Cyclops* the paternal and maternal chromatin-groups not only remain distinctly separated during the anaphase, but give rise to double nuclei in the two-cell stage (Fig. 146). Each half again gives rise to a separate group of chromosomes at the second cleavage, and this is repeated at least as far as the blastula stage. Herla and Zoja have shown furthermore that if in *Ascaris* the egg of variety *bivalens*, having two chromosomes, be fertilized with the spermatozoön of variety *univalens* having one chromosome, the three chromosomes reappear at each cleavage, at least as far as the twelve-cell stage (Fig. 145); and according to Zoja, the paternal chromosome is distinguishable from the two maternal at each step by its smaller size. We have thus what must be reckoned as more than a possibility, that every cell in the body of the child may receive from each parent not only half of its chromatin-substance, but one-half of its chromosomes, as distinct and individual descendants of those of the parents.

---

[1] '89, pp. 10, 33.

C. The Centrosome in Fertilization

In examining more critically the history of the centrosomes we may conveniently take Boveri's hypothesis of fertilization as a point of departure, since it has long formed the focus of discussion of the entire subject. Before the hypothesis is more closely scrutinized we may first eliminate two other views, both of which are irreconcilable with it, though neither has stood the test of later research. The first of these, doubtfully suggested by Van Beneden ('87) and definitely maintained by Wheeler ('97) in the case of *Myzostoma*, is that the cleavage-centrosomes have no definite relation to the spermatozoön, but are derived from the egg — a conclusion that has the *a priori* support of the fact that in parthenogenesis the centrosomes are certainly of maternal origin.

Van Beneden's early statement may be passed by, since it was no more than a surmise. Wheeler, after a careful research, found that no sperm-aster accompanied the sperm-nucleus — a fact correlated with the absence of a middle-piece in the spermatozoön, — and reached the conclusion that after formation of the polar bodies, the egg-centrosomes persisted to become directly converted into the cleavage-centrosomes (Fig. 104). That the absence of a distinct middle-piece is not a valid argument is shown by the insect-spermatozoön, where the region of the middle-piece is likewise not marked off from the tail, yet as we have seen (p. 165) the centrosome passes into this part of the spermatozoön. Kostanecki's later examination of the fertilization of the same animal ('98), while inconclusive on the main point, leaves little doubt that Wheeler's evidence was equally so; for he has on the one hand shown that the sperm-nucleus is often accompanied by a sperm-

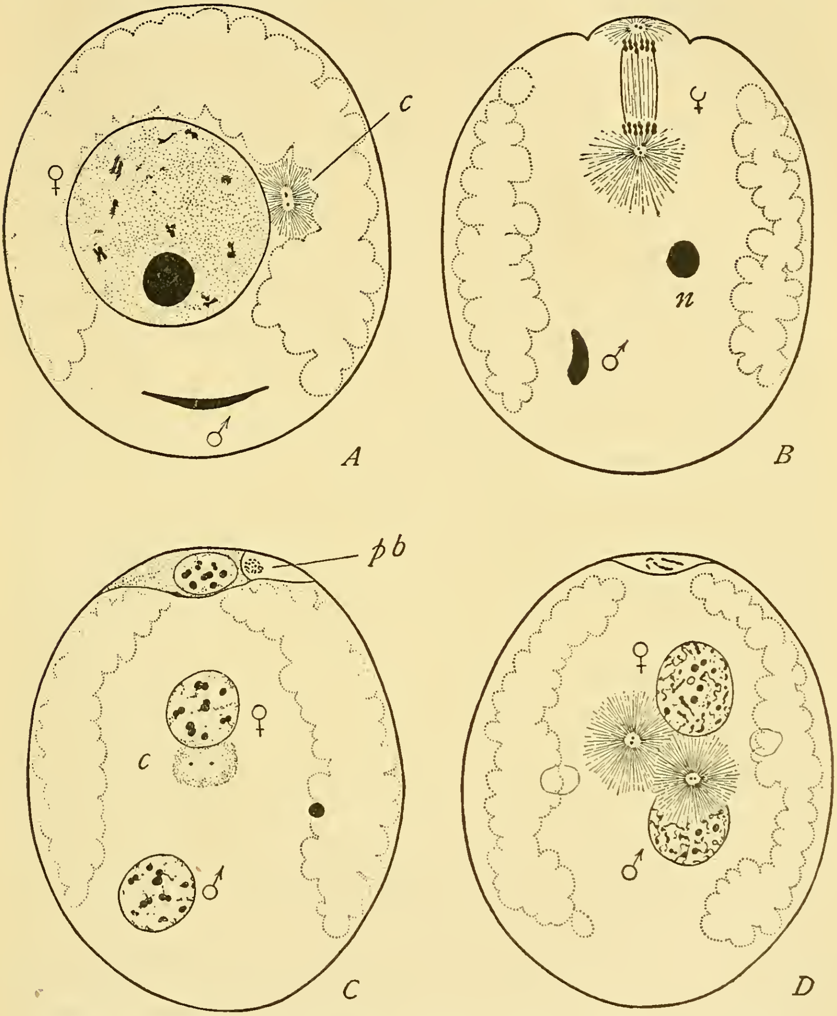

Fig. 104. — Fertilization of the egg of the parasitic annelid, *Myzostoma*. [WHEELER.]

A. Soon after entrance of the spermatozoön; the sperm-nucleus at ♂; at ♀ the germinal vesicle; at *c* the double centrosome. *B*. First polar body forming at ♀; *n*. the cast-out nucleolus or germinal spot. *C*. The polar bodies formed (*p.b.*); germ-nuclei of equal size; at *c* the centrosomes. *D*. Approach of the germ-nuclei; the amphiaster formed.

aster containing a pair of centrosomes, on the other hand that these, like the egg-centrosomes, wholly disappear from view at a later period, the cleavage-centrosomes having only a conjectural origin.

The second of the views in question is that the cleavage-centrosomes are derived from both germ-cells; and this in turn has in its favour the *a priori* evidence that in the Infusoria conjugation takes place between two mitotic figures (p. 224). It appears in two forms, of which the first, though undoubtedly erroneous, has had so interesting a history as to deserve a brief review. It was predicted by Rabl in 1889 that if the centrosome be a permanent cell-organ, the conjugation of germ-cells and germ-nuclei would be found to involve also a conjugation of centrosomes. Unusual interest was therefore aroused when Fol, in 1891, under the somewhat dramatic title of the "Quadrille of Centres," described precisely such a conjugation of centrosomes as Rabl had predicted. The results of this veteran observer were very positively and specifically set forth, and were of so logical and consistent a character as to command instant acceptance on the part of many authorities. In the eggs of the sea-urchin the sperm-centrosome and egg-centrosome were asserted to divide each into two, the daughter-centrosomes then conjugating two and two, paternal with maternal, to form the cleavage-centrosomes. The same result was announced by Guignard ('91) in the lily, by Conklin ('93) in the gasteropod *Crepidula*, less definitely by Blanc ('93) in the trout, and still later by Van der Stricht ('95) in *Amphioxus*. None of these results have stood the test of later work. Fol's result was opposed to the earlier conclusions of Boveri and Hertwig, and a careful reëxamination of the fertilization of the echinoderm egg, independently made in 1894–95 by Boveri (*Echinus*), by myself (*Toxopneustes*), and Mathews (*Arbacia*, *Asterias*), and slightly later by Hill ('95) and Reinke ('95) in *Sphærechinus*, demonstrated its erroneous character. Various attempts have been made to explain Fol's results as based on double-fertilized eggs, on imperfect method, on a misinterpretation of the double centrosomes of the cleavage-spindle, yet they still remain an inexplicable anomaly of scientific literature.

Serious doubt has also been thrown on Conklin's conclusions by subsequent research. Kostanecki and Wierzejski ('96) made a very thorough study, by means of serial sections, of the fertilization of the gasteropod *Physa*, and reached exactly the same result as that obtained in the echinoderms. Here, also, the egg-centres degenerate, their place being taken by a new pair, arising in intimate relation with the middle-piece of the spermatozoön, about which forms a sperm-amphiaster (Fig. 89). Conklin, after renewed research, himself admitted that no quadrille occurs in *Crepidula*, though he still believes that a union of paternal and maternal attraction-spheres takes place.

Guignard's results, too, have entirely failed of confirmation by later observers (p. 221), and in his own latest contribution to the subject ('99) the centrosomes are conspicuous by their absence in both the text and the figures. In like manner Van der Stricht's conclusions have been shown by Sobotta ('97) to be without substantial foundation, while Blanc's account, opposed to the earlier work of Böhm, is too incomplete to carry any weight. The entire case for the "quadrille" has thus fallen to the ground. In its second form the supposed double origin of the centrosomes rests upon a single research upon *Ascaris* by Carnoy and Le Brun ('97, 2), who assert that the cleavage-centrosomes arise *de novo* and separately, one inside of each of the germ-nuclei, to migrate thence out into the cytoplasm. At the close of mitosis they wholly disappear, to be replaced by a new pair, likewise of intranuclear origin. Since this result is totally opposed to those of Van Beneden, Boveri, Erlanger, and Kostanecki and Siedlecki on the same object, and is contradicted in the most positive manner by Fürst,[1] it may be received with some scepticism. The work of Kostanecki and Siedlecki ('96) demonstrates the division of the sperm-centrosome in *Ascaris* as described by Boveri; and while it still remains possible that the daughter-centrosomes may for a very brief period disappear (as in some of the mollusks described beyond), no ground is given for such a conclusion as Carnoy has drawn. No one familiar with the object can repress the suspicion that Carnoy and Le Brun have confused the centrosomes with the nucleoli; but only renewed research can determine the point.

The ground is now clear for a closer study of Boveri's hypothesis in the light of more recent research. It should first be pointed out that that hypothesis is based upon and forms a part of the more general theory of the autonomy of the centrosome; and if the latter theory cannot be sustained, the *a priori* side of Boveri's hypothesis assumes a different aspect. In point of fact the general outcome of recent research on fertilization has been on the whole unfavourable to the view that the cleavage-centrosomes must necessarily be individually identical with permanent preëxisting centrosomes — indeed, it is in this very field that some of the most convincing evidence against the persistence of the centrosome has been produced. The mode of origin of the cleavage-centrosomes is nevertheless a question of high interest on account of the unmistakable genetic relations existing between the centrosome of the spermatid and spermatozoön and those of the sperm-amphiaster within the egg.

There are two points of capital importance to be determined before a definite decision regarding the origin of the cleavage-centrosomes can be reached. First, are the centrosomes of the sperm-aster within the egg identical with, or the descendants of, a centrosome or pair of centrosomes in the middle-piece of the spermatozoön? Second, do they actually persist to form those of the cleavage-amphiaster? In the present state of knowledge we are not in a position to give an affirmative answer to the first of these questions. As has been shown in Chapter III., it is no longer possible to doubt that the middle-piece either contains or is itself a metamorphosed centrosome; but, as pointed out at page 196, it does not seem possible that the extremely minute centrosome of the sperm-aster can represent the entire centrosome of the middle-piece (however we conceive the origin of the latter). At most we can only assume that a part of the latter persists as the sperm-centrosome within the egg. The exact origin of the latter still remains problematical. A large number of observers are now agreed that the sperm-aster is formed about a focus that is either in or very near the middle-piece;[1] but no one, I believe, has yet succeeded in showing that the centrosome actually is the metamorphosed middle-piece, or escapes from it.[2] The possibility therefore remains that the centrosome of the sperm-aster is not actually imported as such into the egg, but is either only a portion of the original spermatid-centrosome, or, as was first suggested by Miss Foot ('97) and further discussed by Mead ('98, 2), is, like the aster, formed anew in the egg-cytoplasm. If the latter alternative be the case, the original form of Boveri's hypothesis would have to be abandoned;

---

[1] '98, p. 105.

---

[1] For example, in echinoderms (Flemming, '81, O. and R. Hertwig, '86, Boveri, '95, Wilson and Mathews, '95, Hill, '95, Reinke, '95, R. Hertwig, '96, Doflein, '97, 2, Erlanger, '98), in *Pterotrachea* and *Pieris* (Henking, '91, '92), in the axolotl (Fick, '93), and *Triton* (Michælis, '97), in *Phallusia* (Hill, '95), in *Ophryotrocha* (Korschelt, '95), in *Physa* (Kostanecki and Wierzejski, '96), in *Strongylus* (Meyer, '95), in *Thysanozoön* (Van der Stricht, '98), and *Prosthiostomum* (Francotte, '98). In a large number of other cases the sperm-aster is found near the sperm-nucleus, but its relation to the middle-piece has not been demonstrated.

[2] I myself formerly concluded ('95, 2) that the entire middle-piece of echinoderms is the centrosome — a result apparently confirmed in a most positive manner by Erlanger ('98), as well as by R. Hertwig ('96) and Doflein ('97, 2). I have, however, demonstrated this to be an error, showing that the extremely minute centrosome is quite distinct from the middle-piece, the latter being thrown aside and degenerating in the egg-cytoplasm outside of the newly formed sperm-aster (Figs. 12, 94). This fact, of which the phenomena in *Toxopneustes* leave no doubt (see Wilson, '97, '99), is, I think, fatal to Kostanecki's and Wierzejski's theory of fertilization ('96, pp. 374–375), according to which the archoplasm of the middle-piece gives rise to the new astral system and is thus the essential fertilizing substance (the centrosome being merely a mechanical centre for the attachment of the rays); but the most careful examination has still failed to show whether the centrosome actually escapes from the middle-piece, nor have other observers had better success with any animal. Erlanger ('96, 2, '97, 4) believes he has seen the centrosome in the *Ascaris* spermatozoön as a distinct body lying behind the nucleus, and that it can be traced continuously into the egg and after its division into the two poles of the cleavage-figure. Neither the schematic figures of his preliminary nor the photographic ones of his final paper seem sufficient to establish either the identity or the subsequent history of the granule in question.

though in substance it would still retain an element of truth, as pointed out beyond.

We may now examine the question whether the sperm-centrosomes are actually identical with the cleavage-centrosomes. That such is the case is positively maintained in the case of *Ascaris* by Boveri, Kostanecki, and Erlanger, in *Physa* by Kostanecki and Wierzejski ('96), in *Thalassema* by Griffin ('96, '99), and in *Chætopterus* by Mead ('95, '98). The two last-mentioned observers, who have followed the phenomena with especial care, produce very strong evidence that at no time do the sperm-centrosomes and asters disappear, and that the former may be traced in unbroken continuity from the time of their first appearance to the daughter-cells resulting from the first cleavage (Figs. 99, 155). On the other hand, a considerable number of observers, beginning with Hertwig (*Phyllirrhoë*, *Pterotrachea*, '75), have found that as the sperm-nucleus enlarges the sperm-asters diminish in size, until, in many cases, they nearly or quite disappear; for example, in *Prostheceræus* (Klinckowström, '97), in the mouse (Sobotta, '95), in *Pleurophyllidia* (MacFarland, '97), *Physa* (Kostanecki and Wierzejski, '96), *Arenicola* (Child, '97), *Unio* (Lillie, '97), *Myzostoma* (Kostanecki, '98), and *Cerebratulus* (Coe, '98).[1] Several of these observers (Klinckowström, MacFarland, Lillie, Child) have found that not only the asters *but also the centrosomes* totally disappear about the time the germ-nuclei come together, a new pair of cleavage-centrosomes and asters being afterward developed at the poles of the united nuclei. These conclusions, if correct, place in a new light the disappearance of the egg-centrosomes; for this process would thus seem to be of the same nature as the disappearance of the sperm-centrosomes, and both Boveri's theory of fertilization and the general hypothesis of the permanence of the centrosomes would receive a serious blow.

---

[1] Coe has pointed out that the eggs of various animals may be arranged in a series showing successive graduations in the disappearance of the sperm-asters. "At the head of the series we must place the eggs of *Ascaris* and *Myzostoma* (according to Kostanecki) and similar ones in which the sperm-asters make their appearance only a short time before the formation of the cleavage-spindle, and which, consequently, suffer no diminution in size. Following these are the eggs of *Chætopterus* (Mead) and *Ophryotrocha* (Korschelt) and of some echinoderms in which the sperm-asters develop very early, but are not described as decreasing in size before the formation of the cleavage-spindle. Then come the eggs of *Toxopneustes* (Wilson) and *Thalassema* (Griffin), where the sperm-asters appear early and develop to a very considerable size, but nevertheless become very much smaller and less conspicuous after the germ-nuclei have come together. After these we must place the eggs of *Physa* (Kostanecki and Wierzejski), for here the sperm-asters, after becoming very large and conspicuous, degenerate to such an extent that only a very few exceedingly delicate fibres remain. Those of *Cerebratulus* follow next.

"Here the sperm-asters increase in size until they extend throughout the whole body of the cell, but at the time of fusion of the germ-nuclei they degenerate completely. The peripheral portions of their fibres, however, may be followed, as stated above of *Pleurophyllidia*, *Prostheceræus*, etc., where the sperm-asters degenerate soon after their formation, so that for a considerable period the egg is without trace of aster-fibres. Yet in all of those cases where the sperm-asters disappear and their centrosomes become lost among the other granules of the cell, we are justified in believing that the sperm-centrosomes nevertheless retain their identity, and later reappear in the cleavage-asters" ('98, p. 455).

The investigators to whom these observations are due have ranged themselves in two groups in the interpretation of the phenomena. On the one hand, Lillie and Child do not hesitate to maintain that the centrosomes actually go out of existence as such, to be re-formed like the asters out of the egg-substance; and that such a new formation of centrosomes is possible seems to be conclusively shown by the experiments of Morgan and Loeb described at pages 215 and 307. On the other hand, Sobotta, MacFarland, Kostanecki, and Coe, relying partly on the analogy of other forms, partly on the occasional presence of the centrosomes during the critical stage, urge that the disappearance of the sperm-centrosomes is only apparent, and is due to the disappearance of the asters, which renders difficult or impossible the identification of the centrosomes among the other protoplasmic granules of the egg. These authors accordingly still uphold Boveri's theory.

It is difficult to sift the evidence at present, for it has now become very important to reëxamine, in the light of these facts, those cases in which the absolute continuity of the centrosome has been maintained — for example, in *Ascaris*, *Chætopterus*, and *Thalassema* — in order to determine whether there may not be here also a brief critical period in which the centrosomes disappear. There are, however, some facts which tend to sustain the conclusion that even though the sperm-centrosomes disappear from view, there is some kind of genetic continuity between them and the cleavage-centrosomes. First, both Kostanecki and Wierzejski ('96) and Coe ('98) have found that there is some variation in eggs apparently equally well preserved, a few individuals showing the sperm-centrosomes at the poles of the united nuclei at the same period when they are invisible in other individuals. Second, both these observers, Coe most clearly, have shown that the egg-centrosomes disappear considerably earlier than the sperm-centrosomes, and Coe has traced the sperm-centrosomes continuously *to the exact points* (*the poles of the united nuclei*) *at which the cleavage-centrosomes afterward appear* (Fig. 155). This important observation leads to the suspicion that the apparent disappearance of the centrosomes may be due to a loss of staining-capacity at the critical period, or that even though the formed centrosome disappears its substance reappears in its successor. Here again we come to the view suggested at page 111, that the centrosome may be regarded as the vehicle of a specific chemical substance which is transported to the nuclear poles by its division, and may there persist even though the body of the centrosome be no longer visible. On such a basis we may perhaps find a reconciliation between these observations and Boveri's theory, and may even bring the fertilization of plants into relation with it (p. 221). Even in case of the nucleus, universally recognized as a permanent cell-organ, it is not the whole structure that persists as such during division, but only the chromatin-substance — in some cases only a small fraction of that substance. The law of genetic continuity therefore would not fail in case of the centrosome, though only a portion of its substance were handed on by division; and even if we take the most extreme negative position, assuming that the sperm-centrosome is wholly formed anew under the stimulus of the spermatozoön, we should still not escape the causal *nexus* between it and the centrosome of the spermatid.

Boveri himself has suggested[1] that the egg may be incited to development by a specific chemical substance carried by the spermatozoön, and the same view has been more recently urged by Mead,[2] while Loeb's recent remarkable experiments on sea-urchins ('99) show that the egg may in this case (*Arbacia*) undergo complete parthenogenetic development as the result of artificial chemical stimulus.[3] Assuming such a substance to exist, by what part of the spermatozoön is it carried? It is possible that the vehicle may be the nucleus, which forms the main bulk of that which enters the egg; and this view seems to be supported by what is at present known of fertilization in the plants (p. 221). Yet when we regard the facts of fertilization in animals, taken in connection with the mode of formation of the spermatozoön, we find it difficult to avoid the conclusion that the substance by which the stimulus to development is normally given is originally derived from the spermatid-centrosome, is conveyed into the egg by the middle-piece, and is localized in the sperm-centrosomes which are conveyed to the nuclear poles during the amphiaster-formation. Accepting such a view, we could gain an intelligible view of the genetic relation between spermatid-centrosome, middle-piece, sperm-centrosome, and cleavage-centrosomes, without committing ourselves to the morphological hypothesis of the persistence of the centrosome as an individualized cell-organ. Such a conclusion, I believe, would retain the substance of Boveri's theory while leaving room for the abandonment of the too simple morphological form in which it was originally cast.

D. FERTILIZATION IN PLANTS

The investigation of fertilization in the plants has always lagged somewhat behind that of the animals, and even at the present time our knowledge of it is rather incomplete. It is, however, sufficient to show that the essential fact is everywhere a union of two germ-nuclei — a process agreeing fundamentally with that observed in animals. On the other hand, almost nothing is known regarding the centrosome and the archoplasmic or kinoplasmic structures; and most recent observations point to the conclusion that in the lowering plants and pteridophytes no centrosomes are concerned in fertilization.

---

[1] '91, p. 431.
[2] '98, 2, p. 217.
[3] *Cf.* p. 111.

Many early observers from the time of Pringsheim ('55) onward described a conjugation of cells in the lower plants, but the union of *germ-nuclei*, as far as I can find, was first clearly made out in the flowering plants by Strasburger in 1877–78, and carefully described by him in 1884. Schmitz observed a union of the nuclei of the conjugating cells of *Spirogyra* in 1879, and made similar observations on other algæ in 1884. Among other forms in which the same phenomenon has been described may be mentioned *Œdigonium* (Klebahn, '92), *Vaucheria* (Oltmanns, '95), *Cystopus* (Wager, '96), *Sphærotheca* and *Erysiphe* (Harper, '96), *Fucus* (Farmer and Williams, '96, Strasburger, '97), *Basidiobolus* (Fairchild, '97), *Pilularia* (Fig. 105, Campbell, '88), *Onoclea* (Shaw, '98, 2), *Zamia* (Webber, '97, 2), and *Lilium* (Guignard, '91, Mottier, '97), *Ginkgo* (Hirase, '97).[1] In all of these forms and many others fertilization is effected by the union of a single paternal and a single maternal uninucleated cell, such as occurs throughout the animal kingdom. There are, however, some apparently well-determined exceptions to this rule occurring in the "compound" multinucleate oöspheres of some of the lower

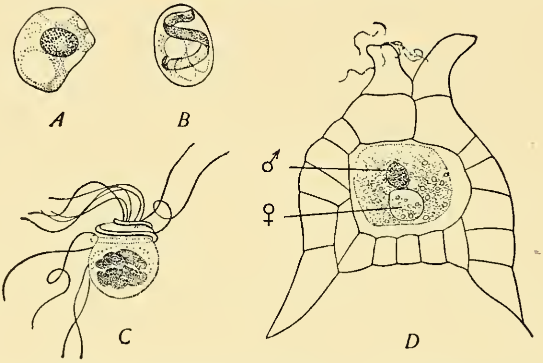

Fig. 105. — Fertilization in *Pilularia*. [CAMPBELL.]

A. B. Early stages in the formation of the spermatozoid. *C.* The mature spermatozoid; the nucleus lies above in the spiral turns; below is a cytoplasmic mass containing starch-grains (*cf.* the spermatozoids of ferns and of *Marsilia*, Fig. 71). *D.* Archegonium during fertilization. In the centre the ovum containing the apposed germ-nuclei (♂, ♀).

---

[1] For unicellular forms see pp. 228, 280.

plants. In *Albugo bliti* (one of the Peronosporeæ), for example, as shown by the recent work of Stevens ('99), the mature ovum contains about a hundred nuclei, and is fertilized by a multinucleate protoplasmic mass derived from the antheridium, each nucleus of the latter conjugating with one of the egg-nuclei. But although the conjugating bodies are here multinucleate, the germ-nuclei conjugate two and two (as is also the case in the multinucleate cysts of *Actinosphærium*, p. 279); and the case therefore forms no real exception to the general rule that one paternal nucleus unites with one maternal.

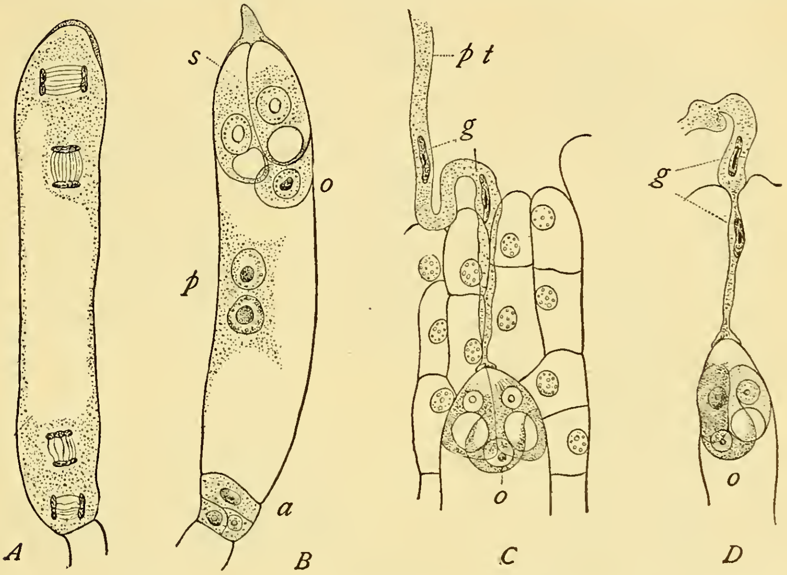

Fig. 106. — Formation of the ovum and penetration of the pollen-tube in flowering plants. [STRASBURGER.]

A. Embryo-sac of *Monotropa*, showing the division that follows the two maturation-divisions and produces the upper and lower "tetrads." *B*. The same, ready for fertilization, showing ovum (*o*), synergidæ (*s*), upper and lower polar cells (*p*), and antipodal cells (*a*). *C*. Penetration of the pollen-tube (*p.t.*) in *Orchis*; *o*. ovum, with synergidæ at either side, *g.n.* generative nuclei in the pollen-tube. *D*. Slightly later stage with generative nuclei entering the micropyle.

Whether a union of more than two germ-nuclei occurs in any of the lower plants is a question still disputed by botanists.[1] Such plural fusion is rendered *a priori* improbable by the observations thus far made upon the one-celled forms both in plants and in animals; and the known facts are sufficient to show that it must be, to say the least, an exceptional process.

In cases where the paternal germ-cell is a ciliated spermatozoid, as in *Fucus*, *Pilularia*, and the ferns and cycads, the germ-nuclei differ more or less widely at the time of union, the sperm-nucleus being smaller, more compact, and deeply staining (Figs. 105, 108), as is the case in such forms of fertilization as the echinoderm-egg. In the case of angiosperms all earlier observers, including Strasburger ('78, '84), Guignard ('91, 1), and Mottier ('97, 1), found the conjugating nuclei to be closely similar at the time of union. The recent observations of Guignard ('99) and Nawaschin ('99) show, however, that even here the sperm-nucleus is smaller, more compact, and of different form (spindle-shaped) from the egg-nucleus (Fig. 107).

---

[1] *Cf.* Hartog, '91, '96, Trow, '95, Stevens, '99, Zimmerman, '96, and literature there cited.

The ovum or oösphere of the flowering plant is a large, rounded cell containing a large nucleus and numerous minute colourless plastids from which arise, by division, the plastids of the embryo (chromatophores, amyloplasts). In the angiosperms the ovum forms one of the eight cells constituting the embryo-sac which morphologically represents the female prothallium or sexual generation of the pteridophyte and is itself embedded in the ovule within the ovary.[1] The male germ-cells are represented in the cycads by two ciliated spermatozoids (p. 175), in the angiosperms by two spindle-shaped "generative nuclei" which are suspected by Guignard and Nawaschin to be motile bodies, though no cilia were seen. These lie near the tip of the pollen-tube (Fig. 107), which is developed as an outgrowth from the pollen-grain and represents a rudimentary male prothallium or sexual generation.[2]

The formation of the pollen-tube, and its growth down through the tissue of the pistil to the ovule, was observed by Amici ('23), Brongniart ('26), and Robert Brown ('31); and in 1833–34 Corda was able to follow its tip through the micropyle into the ovule.[3] Strasburger first demonstrated the fact that the generative nucleus, carried at the tip of the pollen-tube, enters the ovum and unites with the egg-nucleus, and the facts have been since carefully studied by himself, by Guignard, Mottier, Webber, Ikeno, Hirase, and a number of others. In the cycads, according to the last-named two observers, a single spermatozoid enters the egg, its nucleus soon fusing with that of the egg (Fig. 108); and the earlier observers of the angiosperms, including Strasburger ('84, '88) and Guignard ('91, 1), likewise found that only one of the generative nuclei entered the embryo-sac. Guignard and Nawaschin have, however, recently made the remarkable discovery that in *Lilium* and *Fritillaria* both generative nuclei enter the embryo-sac. One of these conjugates with the egg-nucleus and

---

[1] The eight cells are at first arranged in an upper and a lower "tetrad" of four cells each, the former including the ovum, two synergidæ, and an "upper polar cell," the latter a "lower polar cell" and three antipodal cells (Figs. 106, 107); *cf.* p. 263.

[2] *Cf.* p. 264.

[3] It is interesting to note that the botanists of the eighteenth century engaged in the same fantastic controversy regarding the origin of the embryo as that of the zoölogists of the time. Moreland (1703), followed by Etienne François Geoffroy, Needham, and others, placed himself on the side of Leeuwenhoek and the spermatists, maintaining that the pollen supplied the embryo which entered the ovule through the micropyle (the latter had been described by Grew in 1672); and even Schleiden adopted a similar view. On the other hand, Adanson (1763) and others maintained that the ovule contained the germ which was excited to development by an aura or vapour emanating from the pollen and entering through the tracheæ of the pistil.

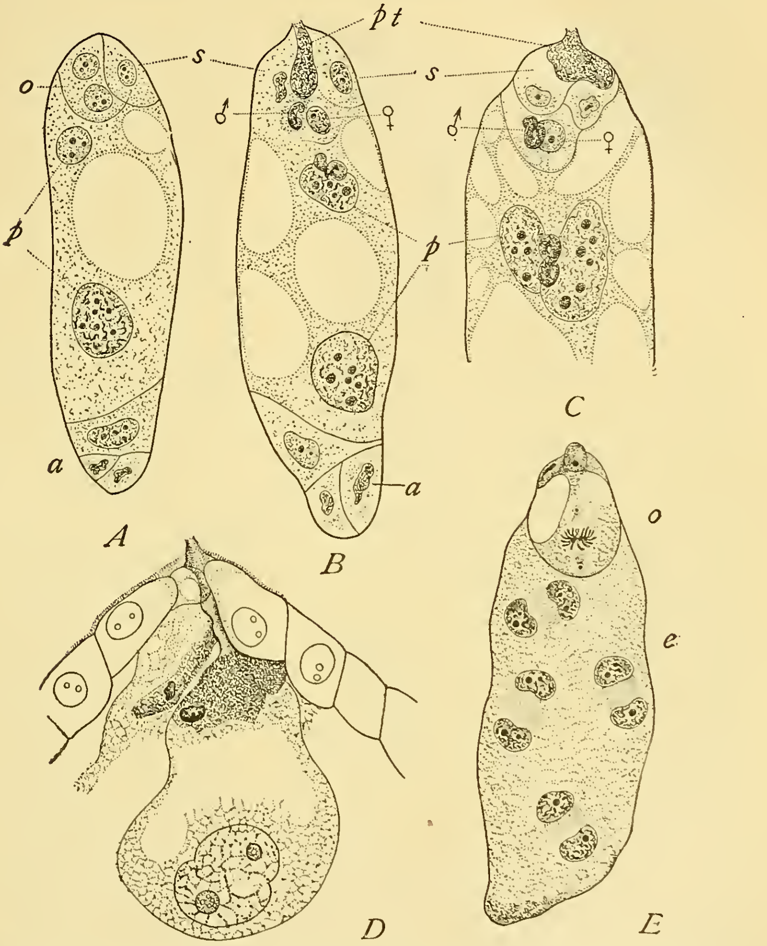

Fig. 107.—Fertilization in the lily. [*D* from MOTTIER, the others from GUIGNARD.]

A. Embryo-sac, ready for fertilization. *B.* Both generative nuclei have entered the embryo-sac; one is approaching the egg-nucleus, the other uniting with the upper polar nucleus. *C.* Union of the germ-nuclei; below, union of the second generative nucleus and the two polar nuclei. *D.* The fertilized egg, showing fusion of the germ-nuclei. *E.* The fertilized egg dividing; below, division of the endosperm-nuclei. *a.* antipodal cells; *e.* endosperm-nuclei; *o.* the oösphere or ovum; *p.* polar nuclei; *p. t.* pollen-tube.

thus effects fertilization (Fig. 107). *The other conjugates with one of the polar nuclei* (usually the upper), which then unites with the other polar nucleus (*cf.* p. 264). By division of the fertilized egg arises the embryo; while by division of the compound nucleus resulting from the fusion of the polar nuclei and the second sperm nucleus are formed the endosperm-cells, which serve for the nourishment of the embryo. This remarkable double copulation within the embryo-sac is without a parallel and is of wholly problematical meaning, but in no way contradicts the general rule regarding the union of two germ-nuclei to produce the embryo.[1]

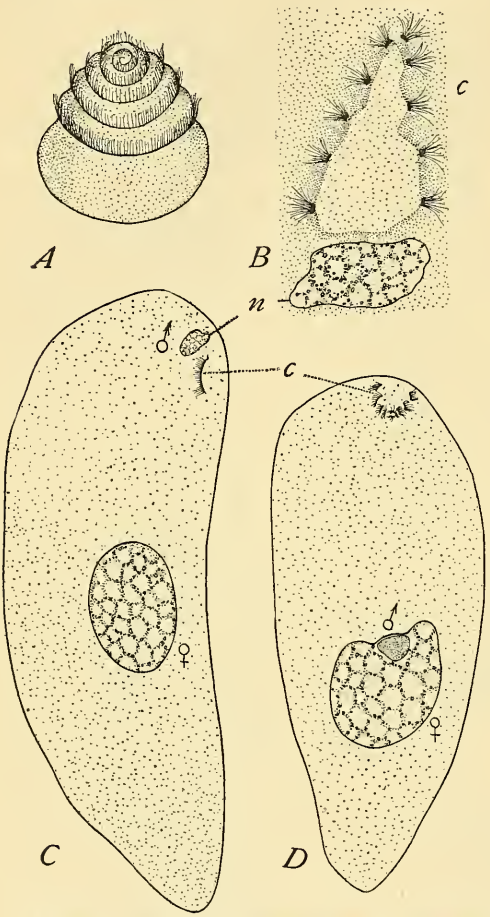

Fig. 108. — Fertilization in a cycad, *Zamia*. [WEBBER.] *A.* Spermatozoid. *B.* The same after entrance into the egg, showing nucleus (*n*) and cilia-bearing band (*c*). *C.* The ovum shortly after entrance of the spermatozoid. *D.* Union of the germ-nuclei, cilia-bearing band near periphery (*c*).

---

[1] As in the case of animals (p. 176), the germ-nuclei of phanerogams also show marked differences in structure and staining-reaction before their union, though they ultimately become exactly equivalent. Thus, according to Rosen ('92, p. 443), on treatment by fuchsin-methyl-blue the male germ-nucleus is "cyanophilous," the female "erythrophilous," as described by Auerbach in animals. Strasburger, while confirming this observation in some cases, finds the reaction to be inconstant, though the germ-nuclei usually show marked differences in their staining-capacity. These are ascribed by Strasburger ('92, '94) to differences in the conditions of nutrition; by Zacharias and Schwarz to corresponding differences in chemical composition, the male nucleus being in general richer in nuclein, and the female nucleus poorer. This distinction disappears during fertilization, and Strasburger has observed, in the case of gymnosperms (after treatment with a mixture of fuchsin-iodine-green), that the paternal nucleus, which is at first "cyanophilous," becomes "erythrophilous," like the egg-nucleus before the pollen-tube has reached the egg. Within the egg both stain exactly alike. These facts indicate, as Strasburger insists, that the differences between the germ-nuclei of plants are, as in animals, of a temporary and non-essential character.

The nature and origin of the achromatic elements involved in the fertilization of plants is still almost wholly in the dark. No observer has yet succeeded in observing either centrosomes or asters in the fertilization of the thallophytes, despite the fact that in some of these forms mitosis takes place with both these structures in a manner nearly analogous to that observed in animals.[1] In the cycads *Zamia* and *Cycas*, Webber and Ikeno ('98) agree that the entire spermatozoid enters, but only the nucleus appears to be concerned in fertilization. The cilia-bearing band — a product of the blepharoplast, and, as described at page 175, probably the analogue of the middle-piece of the animal spermatozoön — remains near the egg-periphery, gives rise to no astral or other fibrillar formations, and apparently remains quite passive (Fig. 108).

In angiosperms, too, the evidence seems to show that no centrosomes are concerned in fertilization. Guignard ('91, 1), in a very detailed and clearly illustrated paper, gave an account of the centrosomes in the lily agreeing almost exactly with the "quadrille of centres" as described by Fol,[2] paternal and maternal centrosomes conjugating two by two. The later and very careful studies of Mottier and others have, however, entirely failed to confirm Guignard's results, the germ-nuclei fusing without the participation of centrosomes or astral formations, and after a time dividing, without centrosomes, in the manner characteristic of the higher plants.[3] Neither in the cryptogams has any one thus far succeeded in finding fertilization-centrosomes or asters at the time the germ-nuclei unite. Strasburger contributes, however, the interesting observation that in *Fucus* the cleavage-centrosomes afterward appear on that side of the cleavage-nucleus derived from the sperm-nucleus, which he believes from analogy may indicate the importation of a "new dynamic centre" into the egg by the spermatozoid.[4] Combining these facts with the phenomena involved in the origin of the spermatozoids, Strasburger suggests that the sperm-nucleus may import into the egg either a formed centrosome (probably thus in *Fucus*) or a certain quantity of "kinoplasm," which incites the mitotic phenomena in the absence of individualized centrosomes.[5] This view harmonizes with that suggested at pages 111 and 214, and we may perhaps here in the end find a reconciliation between the various types, not only of fertilization but also of mitosis, in plants and animals.

On their face the facts of fertilization in plants, especially in the phanerogams, seem to indicate that the stimulus to development is given by the paternal germ-nucleus. Nevertheless, the analogy of animal fertilization would lead us to expect that the fertilizing substance is contained not in the nucleus but in the cytoplasm — more specifically, in the case of spermatozoids, in the cilia-bearing body derived from the blepharoplast, which in its development so strongly suggests a centrosome (p. 172). Webber's and Ikeno's observations on the cycads are not necessarily fatal to this view; for, as I have shown (p. 188), the middle-piece in the echinoderm is likewise cast off and degenerates near the periphery of the egg, and the centrosome is a body far more minute. The possibility has been admitted that this centrosome may be formed *de novo* under the influence of the middle-piece, which itself perishes. In like manner it may also be possible that the primary stimulus in *Zamia* and like cases is given by the cilia-bearing body, even though this body itself disappears and the mitotic apparatus is not formed until long afterward.

---

[1] *Cf.* p. 82.

[2] *Cf.* p. 210.

[3] *Cf.* p. 82.

[4] '97, p. 418.

[5] '97, p. 420.

E. CONJUGATION IN UNICELLULAR FORMS

The conjugation of unicellular organisms possesses a peculiar interest, since it is undoubtedly a prototype of the union of germ-cells in the multicellular forms. Bütschli and Minot long ago maintained that cell-divisions tend to run in cycles, each of which begins and ends with an act of conjugation. In the higher forms the cells produced in each cycle cohere to form the multicellular body; in the unicellular forms the cells separate as distinct individuals, but those belonging to one cycle are collectively comparable with the multicellular body. The validity of this comparison, in a morphological sense, is generally admitted.[1] No process of conjugation, it is true, is known to occur in many unicellular and in some multicellular forms, and the cyclical character of cell-division still remains *sub judice*.[2] It is none the less certain that a key to the fertilization of higher forms must be sought in the conjugation of unicellular organisms.

The difficulties of observation are, however, so great that we are as yet acquainted with only the outlines of the process, and have still no very clear idea of its finer details or its physiological meaning. The phenomena have been most closely followed in the Infusoria by Bütschli, Engelmann, Maupas, and Richard Hertwig, though many valuable observations on the conjugation of unicellular plants have been made by De Bary, Schmitz, Klebahn, and Overton. All these observers have reached the same general result as that attained through study of the fertilization of the egg; namely, that an essential phenomenon of conjugation is *a union of the nuclei of the conjugating cells.* Among the unicellular plants both the cell-bodies and the nuclei completely fuse. Among animals this may occur; but in

---

Cf. p. 58.

[2] *Cf.* p. 178.

many of the Infusoria union of the cell-bodies is only temporary, and the conjugation consists of a mutual exchange and fusion of nuclei. It is impossible within the limits of this work to attempt more than a sketch of the process in a few forms.

We may first consider the conjugation of Infusoria. Maupas's beautiful observations have shown that in this group the life-history

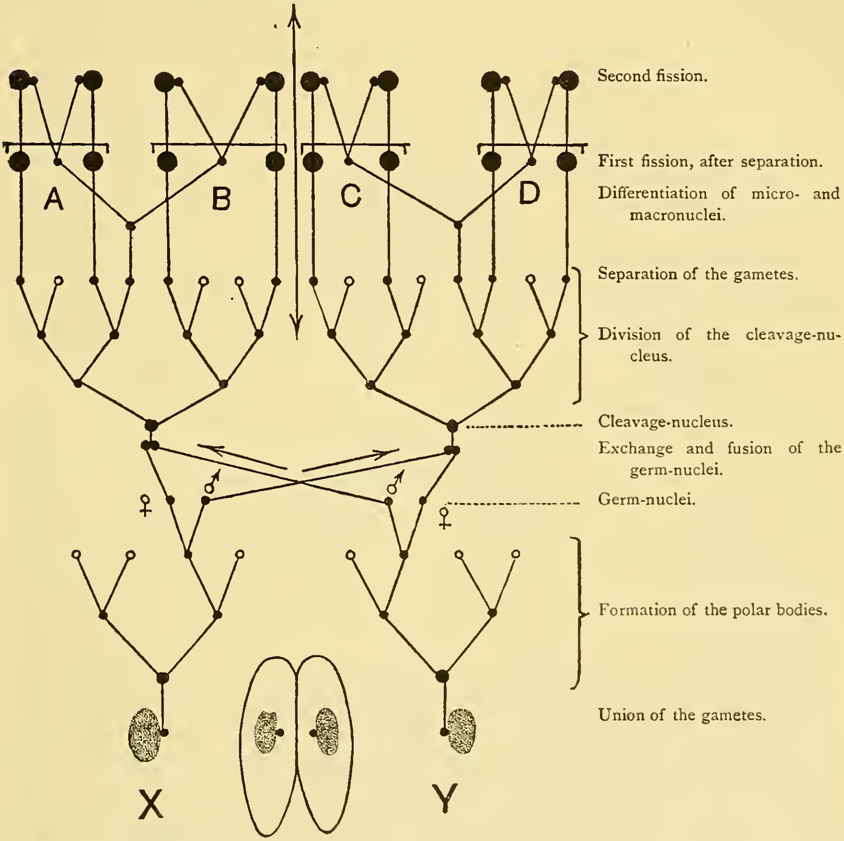
Second fission.
First fission, after separation.
Differentiation of micro- and macronuclei.
Separation of the gametes.
Division of the cleavage-nucleus.
Cleavage-nucleus.
Exchange and fusion of the germ-nuclei.
Germ-nuclei.
Formation of the polar bodies.
Union of the gametes.
A
B
C
D
♀
♂
♂
♀
X
Y

Fig. 109. — Diagram showing the history of the micronuclei during the conjugation of *Paramœcium.* [Modified from Maupas.]

X and *Y* represent the opposed macro- and micronuclei in the two respective gametes; circles represent degenerating nuclei; black dots, persisting nuclei.

of the species runs in cycles, a long period of multiplication by cell-division being succeeded by an "epidemic of conjugation," which inaugurates a new cycle, and is obviously comparable in its physiological aspect with the period of sexual maturity in the Metazoa. If conjugation does not occur, the race rapidly degenerates and dies out; and Maupas believes himself justified in the conclusion that conjugation counteracts the tendency to senile degeneration and causes rejuvenescence, as maintained by Bütschli and Minot.[1]

In *Stylonychia pustulata*, which Maupas followed continuously from the end of February until July, the first conjugation occurred on April 29th, after 128 bi-partitions; and the epidemic reached its height three weeks later, after 175 bi-partitions. The descendants of individuals prevented from conjugation died out through "senile degeneracy," after 316 bi-partitions. Similar facts were observed in many other forms. The degeneracy is manifested by a very marked reduction in size, a partial atrophy of the cilia, and especially by a more or less complete *degradation of the nuclear apparatus*. In *Stylonychia pustulata* and *Onychodromus grandis* this process especially affects the micronucleus, which atrophies, and finally disappears, though the animals still actively swim, and for a time divide. Later, the macronucleus becomes irregular, and sometimes breaks up into smaller bodies. In other cases, the degeneration first affects the macronucleus, which may lose its chromatin, undergo fatty degeneration, and may finally disappear altogether (*Stylonychia mytilus*), after which the micronucleus soon degenerates more or less completely, and the race dies. It is a very significant fact that toward the end of the cycle, as the nuclei degenerate, the animals become incapable of taking food and of growth; and it is probable, as Maupas points out, that the degeneration of the cytoplasmic organs is due to disturbances in nutrition caused by the degeneration of the nucleus.

The more essential phenomena occurring during conjugation are as follows. The Infusoria possess two kinds of nuclei, a large *macronucleus* and one or more small *micronuclei*. During conjugation the macronucleus degenerates and disappears, and the micronucleus alone is concerned in the essential part of the process. The latter divides several times, one of the products, the *germ-nucleus*, conjugating with a corresponding germ-nucleus from the other individual, while the others degenerate as "corpuscules de rebut." The dual nucleus thus formed, which corresponds with the cleavage-nucleus of the ovum, then gives rise by division to both macronuclei and micronuclei of the offspring of the conjugating animals (Fig. 109).

These facts may be illustrated by the conjugation of *Paramœcium caudatum*, which possesses a single macronucleus and micronucleus, and in which conjugation is temporary and fertilization mutual. The two animals become united by their ventral sides and the macronucleus of each begins to degenerate, while the micronucleus divides twice to form four spindle-shaped bodies (Fig. 110, *A*, *B*). Three of these degenerate, forming the "corpuscules de rebut," which play no further part. The fourth divides into two, one of which, the "female pronucleus," remains in the body, while the other, or "male pronucleus," passes into the other animal and fuses with the female pronucleus (Fig. 110, *C–H*). Each animal now contains a cleavage-nucleus equally derived from both the conjugating animals, and the latter soon separate. The cleavage-nucleus in each divides three

---

[1] *Cf.* p. 179.

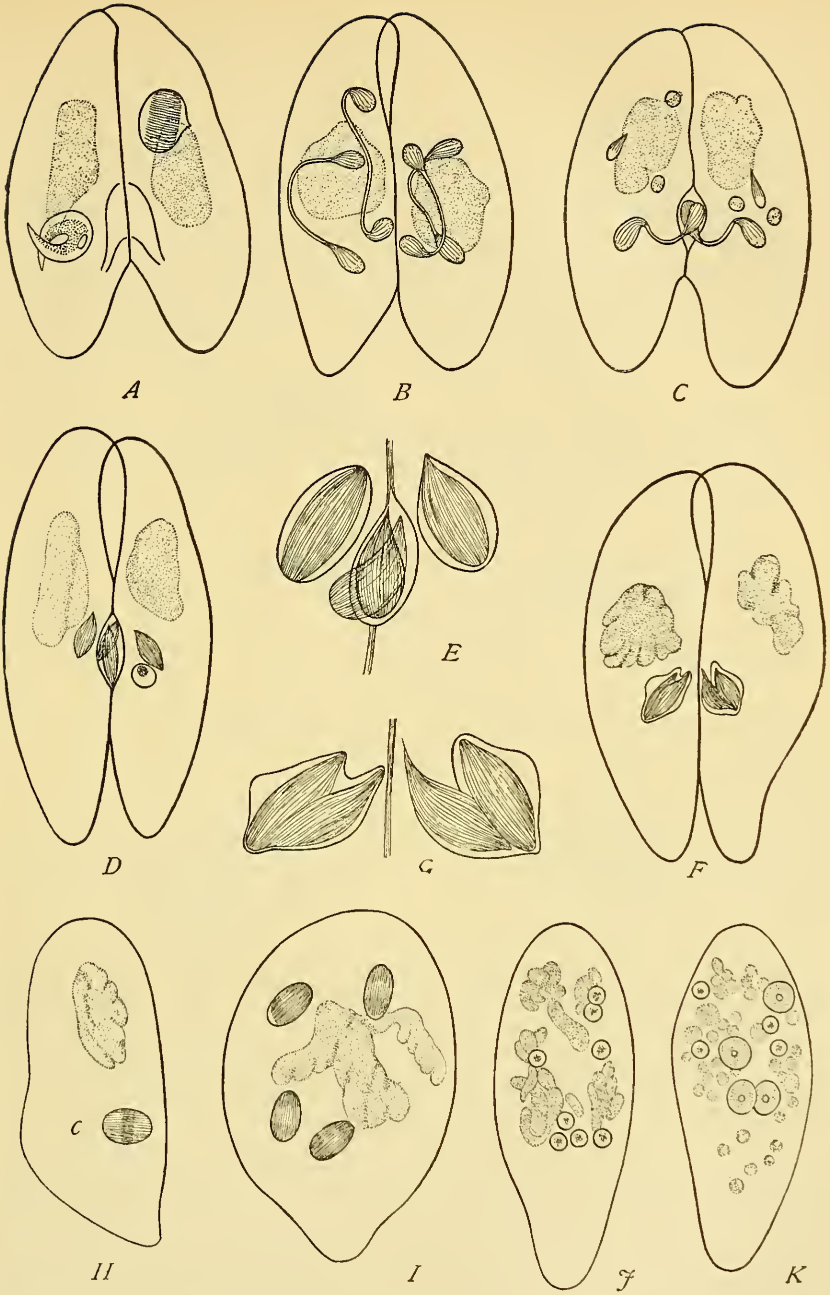

Fig. 110. — Conjugation of *Paramœcium caudatum*. [*A–C*, after R. Hertwig; *D–K*, after Maupas.] (The macronuclei dotted in all the figures.)

A. Micronuclei preparing for their first division. *B*. Second division. *C*. Third division; three polar bodies or "corpuscules de rebut," and one dividing germ-nucleus in each animal. *D*. Exchange of the germ-nuclei. *E*. The same, enlarged. *F*. Fusion of the germ-nuclei. *G*. The same, enlarged. *H*. Cleavage-nucleus, (*c*) preparing for the first division. *I*. The cleavage-nucleus has divided twice. *J*. After three divisions of the cleavage-nucleus; macronucleus breaking up. *K*. Four of the nuclei enlarging to form new macronuclei. The first fission soon takes place.

times successively, and of the eight resulting bodies four become macronuclei and four micronuclei (Fig. 110, *H–K*). By two succeeding fissions the four macronuclei are then distributed, one to each of the four resulting individuals. In some other species the micronuclei are equally distributed in like manner, but in *P. caudatum* the process is more complicated, since three of them degenerate, and the fourth divides twice to produce four new micronuclei. In either case at the close of the process each of the conjugating individuals has given rise to four descendants, each containing a macronucleus and micronucleus derived from the cleavage-nucleus. From this time forward fission follows fission in the usual manner, both nuclei dividing at each fission, until, after many generations, conjugation recurs.

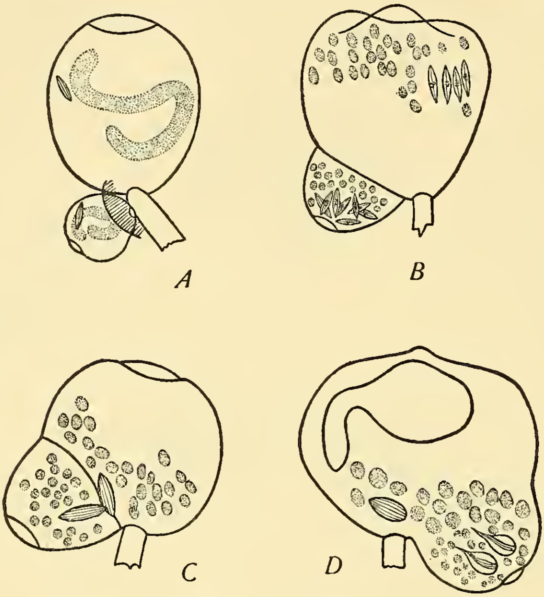

Fig. 111. — Conjugation of Vorticellids. [MAUPAS.]

A. Attachment of the small free-swimming microgamete to the large fixed macrogamete; micronucleus dividing in each (*Carchesium*). *B.* Microgamete containing eight micronuclei; macrogamete four (*Vorticella*). *C.* All but one of the micronuclei have degenerated as polar bodies or "corpuscules de rebut." *D.* Each of the micronuclei of the last stage has divided into two to form the germ-nuclei; two of these, one from each gamete, have conjugated to form the cleavage-nucleus seen at the left; the other two, at the right, are degenerating.

Essentially similar facts have been observed by Richard Hertwig and Maupas in a large number of forms. In cases of permanent conjugation, as in *Vorticella*, where a smaller *microgamete* unites with a larger *macrogamete*, the process is essentially the same, though the details are still more complex. Here the germ-nucleus derived from each gamete is in the macrogamete one-fourth and in the microgamete one-eighth of the original micronucleus (Fig. 111). Each germ-nucleus divides into two, as usual, but one of the products of each degenerates, and the two remaining pronuclei conjugate to form a cleavage-nucleus.

The facts just described show a very close parallel to those observed in the maturation and fertilization of the egg. In both cases there is a union of two similar nuclei to form a cleavage-nucleus or its equivalent, equally derived from both gametes, and this is the progenitor of all the nuclei of the daughter-cells arising by subsequent divisions. In both cases, moreover (if we confine the comparison to the egg), the original nucleus does not conjugate with its fellow until it has by division produced a number of other nuclei all but one of which degenerate. Maupas does not hesitate to compare these degenerating nuclei or "corpuscules de rebut" with the polar bodies (p. 181), and it is a remarkable coincidence that their number, like that of the polar bodies, is often three, though this is not always the case.

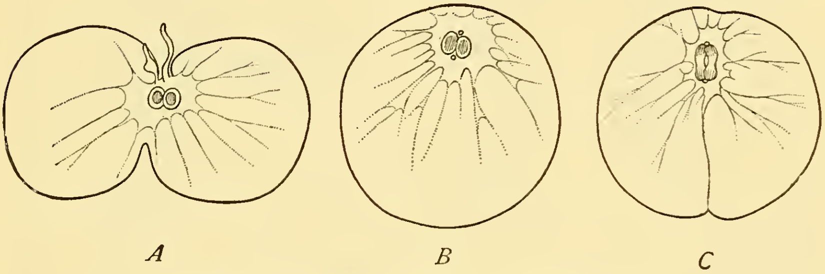

Fig. 112. — Conjugation of *Noctiluca*. [ISHIKAWA.]

A. Union of the gametes, apposition of the nuclei. *B.* Complete fusion of the gametes. Above and below the apposed nuclei are the centrosomes. *C.* Cleavage-spindle, consisting of two separate halves.

A remarkable peculiarity in the conjugation of the Infusoria is the fact that *the germ-nuclei unite when in the form of spindles or mitotic figures.* These spindles consist of achromatic fibres, or "archoplasm," and chromosomes, but no asters or undoubted centrosomes have been thus far seen in them. During union the spindles join side by side (Fig. 110, *G*), and this gives good reason to believe that the chromatin of the two gametes is equally distributed to the daughter-nuclei as in Metazoa. In the conjugation of some other Protozoa the nuclei unite while in the resting state; but very little is known of the process save in the cystoflagellate *Noctiluca*, which has been studied with some care by Cienkowsky and Ishikawa (Fig. 112). Here the conjugating animals completely fuse, but the nuclei are merely apposed and give rise each to one-half of the mitotic figure. At either pole of the spindle is a centrosome, the origin of which remains undetermined.

It is an interesting fact that in *Noctiluca*, in the gregarines, and probably in some other Protozoa, conjugation is followed by a very rapid multiplication of the nucleus followed, by a corresponding division of the cell-body to form "spores," which remain for a time closely aggregated before their liberation. The resemblance of this process to the fertilization and subsequent cleavage of the ovum is particularly striking.

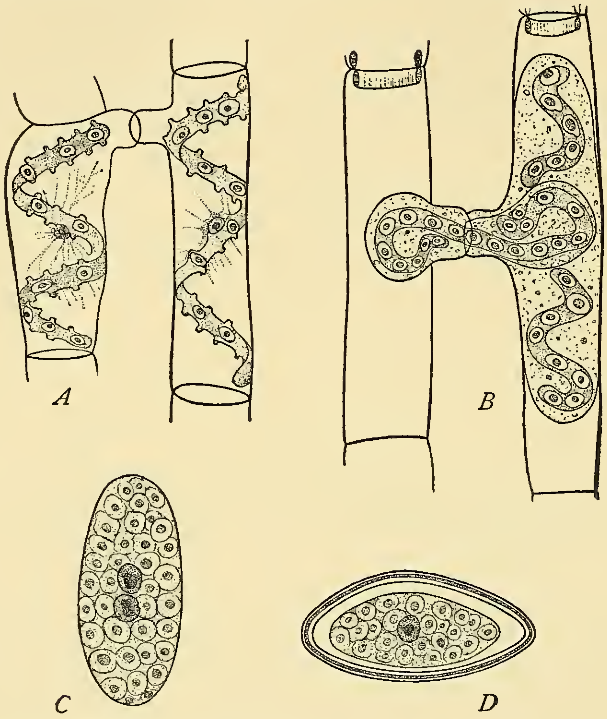

Fig. 113. — Conjugation of *Spirogyra*. [Overton.]

A. Union of the conjugating cells (*S. communis*). *B.* The typical, though not invariable, mode of fusion in *S. Weberi;* the chromatophore of the "female" cell breaks in the middle, while that of the "male" cell passes into the interval. *C.* The resulting zygospore filled with pyrenoids, before union of the nuclei. *D.* Zygospore after fusion of the nuclei and formation of the membrane.

The conjugation of unicellular plants shows some interesting features. Here the conjugating cells completely fuse to form a "zygospore" (Figs. 113, 140), which as a rule becomes surrounded by a thick membrane, and, unlike the animal conjugate, may long remain in a quiescent state before division. Not only do the nuclei unite, but in many cases the plastids also (chromatophores). In *Spirogyra* some interesting variations in this regard have been observed. In some species De Bary has observed that the long band-shaped chromatophores unite end to end so that in the zygote the paternal and maternal chromatophores lie at opposite ends. In *S. Weberi*, on the other hand, Overton has found that the single maternal chromatophore breaks in two in the middle and the paternal chromatophore is interpolated between the two halves, so as to lie in the middle of the zygote (Fig. 113). It follows from this, as De Vries has pointed out, that the origin of the chromatophores in the daughter-cells differs in the two species, for in the former case one receives a maternal, the other a paternal, chromatophore, while in the latter, the chromatophore of each daughter-cell is equally derived from those of the two gametes. The final result is, however, the same; for, in both cases, the chromatophore of the zygote divides in the middle at each ensuing division. In the first case, therefore, the maternal chromatophore passes into one, the paternal into the other, of the daughter-cells. In the second case the same result is effected by two succeeding divisions, the two middle-cells of the four-celled band receiving paternal, the two end-cells maternal, chromatophores. In the case of a *Spirogyra* filament having a single chromatophore it is therefore "wholly immaterial whether the individual cells receive the chlorophyll-band from the father or the mother" (De Vries).[1]

F. Summary and Conclusion

All forms of fertilization involve a conjugation of cells by a process that is the exact converse of cell-division. In the lowest forms, such as the unicellular algæ, the conjugating cells are, in a morphological sense, precisely equivalent, and conjugation takes place between corresponding elements, nucleus uniting with nucleus, cell-body with cell-body, and even, in some cases, plastid with plastid. Whether this is true of the centrosomes is not known, but in the Infusoria there is a conjugation of the achromatic spindles which certainly points to a union of the centrosomes or their equivalents. As we rise in the scale, the conjugating cells diverge more and more, until in the higher plants and animals they differ widely not only in form and size, but also in their internal structure, and to such an extent that they are no longer equivalent either morphologically or physiologically. Both in animals and in plants the paternal germ-cell loses most of its cytoplasm, the main bulk of which, and hence the main body of the embryo, is now supplied by the egg; and in the higher plants, the egg alone retains the plastids which are thus supplied by the mother alone. On the other hand, the paternal germ-cell is the carrier of something which incites the egg to development, and thus constitutes the fertilizing element in the narrower sense. There is strong ground for the conclusion that in the animal spermatozoön this element is, if not an actual centrosome, a body or a substance directly derived from a centrosome of the parent body and contained in the middle-piece. Boveri's theory, according to which fertilization consists essentially of the replacement of a missing or degenerating egg-centrosome by the importation of a sperm-centrosome, was stated in too simple and mechanical a form; for the facts of spermatogenesis show conclusively that the spermatid-centrosome is not simply handed on unmodified by the spermatozoön to the egg, and the theory wholly breaks down in the case of the higher plants. But although the theory probably cannot be sustained in its morphological form, it may still contain a large element of truth when recast in physiological terms. Like mitosis, fertilization is perhaps at bottom a chemical process, the stimulus to development being given by a specific chemical substance carried in some cases by an individualized centrosome or one of its morphological products, in other cases by less definitely formed material. In the case of animals, we cannot ignore the historical continuity shown in the origin of the spermatid-centrosomes, the formation of the middle-piece, and the origin of the sperm-centrosomes and sperm-amphiaster in the egg, even though we do not yet know whether the sperm-centrosome is as such imported into the egg. And this chain of phenomena suggests that even in the higher plants, where no centrosomes seem to occur, the fertilizing substance, even if brought into the egg in an unformed state, may still be genetically related to the mitotic apparatus of the preceding division.[1]

---

[1] De Vries's conclusion is, however, not entirely certain; for it is impossible to determine, save by analogy, whether the chromatophores maintain their individuality in the zygote.

Through the differentiation between the paternal and germ-cells in the higher forms indicated above, their original morphological equivalence is lost and only the nuclei remain of exactly the same value. This is shown by their history in fertilization, each giving rise to the same number of chromosomes exactly similar in form, size, and staining-reactions, equally distributed by cleavage to the daughter-cells, and probably to all the cells of the body. *We thus find the essential fact of fertilization and sexual reproduction to be a union of equivalent nuclei; and to this all other processes are tributary.*

As regards the most highly differentiated type of fertilization and development we reach therefore the following conception. From the mother comes in the main the cytoplasm of the embryonic body which is the principal substratum of growth and differentiation. From both parents comes the hereditary basis or chromatin by which these processes are controlled and from which they receive the specific stamp of the race. From the father comes the stimulus inducing the organization of the machinery of mitotic division by which the egg splits up into the elements of the tissues, and by which each of these elements receives its quota of the common heritage of chromatin. Huxley hit the mark two score years ago when in the words that head this chapter he compared the organism to a web of which the warp is derived from the female and the woof from the male. Our principal advance upon this view is the knowledge that this web is probably to be sought in the chromatic substance of the nuclei; and perhaps we shall not push the figure too far if we compare the amphiaster to the loom on which the fabric is woven.

---

[1] *Cf.* Strasburger's view, p. 221.

LITERATURE. IV[1]

Van Beneden, E. — Recherches sur la maturation de l'œuf, la fécondation et la division cellulaire: *Arch. Biol.*, IV. 1883.

Van Beneden and Neyt. — Nouvelles recherches sur la fécondation et là division mitosique chez l'Ascaride mégalocephale: *Bull. Acad. roy. de Belgique*, III. 14, No. 8. 1887.

Boveri, Th. — Über den Anteil des Spermatozoön an der Teilung des Eies: *Sitz.-Ber. d. Ges. f. Morph. u. Phys. in München*, B. III., Heft 3. 1887.

Id. — Zellenstudien, II. 1888.

Id. — Befruchtung: *Merkel und Bonnet's Ergebnisse*, I. 1891.

Id. — Über das Verhalten der Centrosomen bei der Befruchtung des Seeigeleies. etc.: *Verhandl. Phys. Med. Ges. Wurzburg*, XXIX. 1895.

Bütschli, O. — Studien über die ersten Entwicklungsvorgänge der Eizelle, *u. s. w.*: *Abh. Senckenb. Ges.*, X. 1876.

Coe, W. R., 99. The Maturation and Fertilization of the Egg of Cerebratulus: *Zool. Jahrb.*, XII.

Fick, R. — Über die Reifung und Befruchtung des Axolotleies: *Zeitschr. Wiss. Zoöl.*, LVI. 4. 1893.

Griffin, B. B. — Studies on the Maturation, Fertilization, and Cleavage of Thalassema and Zirphæa: *Journ. Morph.*, XV. 1899.

Guignard, L. — Nouvelles études sur la fécondation: *Ann. d. Sciences nat. Bot.*, XIV. 1891.

Hartog, M. M. — Some Problems of Reproduction, etc.: *Quart. Journ. Mic. Sci.*, XXXIII. 1891.

Hertwig, O. — Beiträge zur Kenntniss der Bildung, Befruchtung und Teilung des tierischen Eies, I.: *Morph. Jahrb.*, I. 1875.

Hertwig, R. — Über die Konjugation der Infusorien: *Abh. d. bayr. Akad. d. Wiss.*, II. Cl. XVII. 1888–89.

Id. — Über Befruchtung und Konjugation: *Verh. deutsch. Zoöl. Ges. Berlin*, 1892.

---

[1] See also Literature, V., p. 287.

Kostanecki, K. v., and Wierzejski, A. — Über das Verhalten der sogen. achromatischen Substanzen im befruchteten Ei: *Arch. mik. Anat.*, XLVII. 2. 1896.

Mark, E. L. — Maturation, Fecundation, and Segmentation of *Limax campestris: Bull. Mus. Comp. Zoöl. Harvard College, Cambridge, Mass.*, VI. 1881.

Maupas. — Le rejeunissement karyogamique chez les Ciliés: *Arch. d. Zoöl.*, 2^{me} série. VII. 1889.

Mead, A. D. — The Origin and Behaviour of the Centrosomes of the Annelid Egg: *Journ. Morph.*, XIV. 2. 1898.

Rückert, J. — Über das Selbständigbleiben der väterlichen und mütterlichen Kernsubstanz während der ersten Entwicklung des befruchteten Cyclops-Eies: *Arch. mik. Anat.*, XLV. 3. 1895.

Strasburger, E. — Neue Untersuchungen über den Befruchtungsvorgang bei den Phanerogamen, als Grundlage für eine Theorie der Zeugung. *Jena*, 1884.

Id. — Über Kern- und Zellteilung im Pflanzenreich, nebst einem Anhang über Befruchtung. *Jena*, 1888. (See Literature II.)

Vejdovský, F. — Entwickelungsgeschichtliche Untersuchungen, Heft 1, Reifung, Befruchtung und Furchung des Rhynchelmis-Eies. *Prag*, 1888.

Waldeyer, W. — Befruchtung und Vererbung: *Verh. Ges. deutsch. Naturf. u. Aerzte*, LXIX. 1897.

Wilson, Edm. B. — Atlas of Fertilization and Karyokinesis. *New York*, 1895.

Zoja, R. — Stato Attuale degli Studi sulla Fecondazione: *Boll. Scientif. di Pavia*, XVIII., XIX. 1896–97.

CHAPTER V

OÖGENESIS AND SPERMATOGENESIS. REDUCTION OF THE CHROMOSOMES

> "Es kommt also in der Generationenreihe der Keimzelle irgendwo zu einer Reduktion der ursprünglich vorhandenen Chromosomenzahl auf die Hälfte, und diese *Zahlen*-reduktion ist demnach nicht etwa nur ein theoretisches Postulat, sondern eine Thatsache."
>
> BOVERI.[1]

VAN BENEDEN'S epoch-making discovery that the nuclei of the conjugating germ-cells contain each one-half the number of chromosomes characteristic of the body-cells has now been extended to so many plants and animals that it may probably be regarded as a universal law of development. The process by which the reduction in number is effected, forms the most essential part of the phenomena of *maturation* by which the germ-cells are prepared for their union. No phenomena of cell-life possess a higher theoretical interest than these. For, on the one hand, nowhere in the history of the cell do we find so unmistakable and striking an adaptation of means to ends or one of so marked a prophetic character, since maturation looks not to the present but to the future of the germ-cells. On the other hand, the chromatin-reduction suggests questions relating to the morphological constitution of nucleus and chromatin, which have an important bearing on all theories of the ultimate structure of living matter and now stand in the foreground of scientific discussion among the most debatable and interesting of biological problems.

Two fundamentally different views have been held of the manner in which the reduction is effected. The earlier and simpler view, which was suggested by Van Beneden and adopted in the earlier works of Weismann, Boveri, and others, assumed an actual degeneration or casting out of half of the chromosomes during the growth of the germ-cells — a simple and easily intelligible process. Later researches conclusively showed, however, that this view cannot be sustained, and that *reduction is effected by a rearrangement and redistribution of the nuclear substance* without loss of any of its essential constituents. It is true that a large amount of chromatin is lost during the growth of the egg.[2] It is nevertheless certain that this loss is not directly connected with the process of reduction; for, as Hertwig and others have shown, no such loss occurs during spermatogenesis, and even in the oögenesis the evidence is clear that an explanation must be sought in another direction. The attempts to find such an explanation have led to some of the most interesting researches of modern cytology; and though only partially successful, they have raised many new questions which promise to give in the end a deeper insight into some of the fundamental questions of cell-morphology. For this reason they deserve careful consideration, despite the fact that taken as a whole the subject still remains an unsolved riddle in the face of which we can only return again and again to Boveri's remark that whatever be its theoretical interpretation the numerical reduction of the chromosomes is itself not a theory but a fact.

---

[1] *Zellenstudien*, III., p. 62.

[2] *Cf.* Figs. 97, 116.

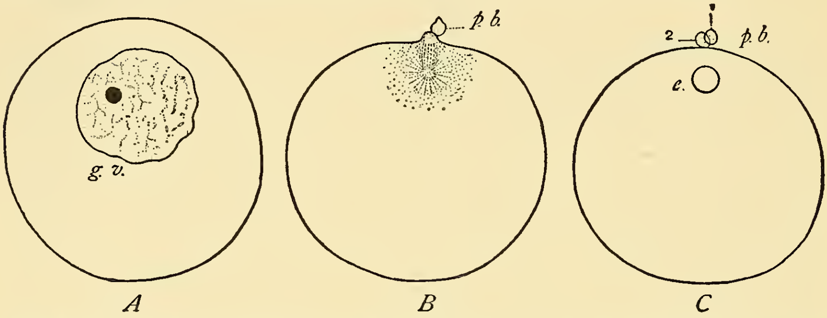

Fig. 114. — Formation of the polar bodies before entrance of the spermatozoön, as seen in the living ovarian egg of the sea-urchin, *Toxopneustes* (× 365).

A. Preliminary change of form in the germinal vesicle. *B.* The first polar body formed, the second forming. *C.* The ripe egg, ready for fertilization, after formation of the two polar bodies (*p. b.* 1, 2); *e.* the egg-nucleus. In this animal the first polar body fails to divide. For its division see Fig. 89.

A. General Outline

The general phenomena of maturation fall under two heads: viz. *oögenesis*, which includes the formation and maturation of the ovum, and *spermatogenesis*, comprising the corresponding phenomena in case of the spermatozoön. Recent research has shown that maturation conforms to the same type in both sexes, which show as close a parallel in this regard as in the later history of the germ-nuclei. Stated in the most general terms, this parallel is as follows:[1] In both sexes the final reduction in the number of chromosomes is effected in the course of the last two cell-divisions, or *maturation-divisions*, by which the definitive germ-cells arise, each of the four cells thus formed having but half the usual number of chromosomes. In the female but one of the four cells forms the "ovum" proper, while the other three, known as the *polar bodies*, are minute, rudimentary, and incapable of development (Figs. 89, 97, 114). In the male, on the other hand, all four of the cells become functional spermatozoa. This difference between the two sexes is probably due to the physiological division of labour between the germ-cells, the spermatozoa being motile and very small, while the egg contains a large amount of protoplasm and yolk, out of which the main mass of the embryonic body is formed. In the male, therefore, all of the four cells may become functional; in the female the functions of development have become restricted to but one of the four, while the others have become rudimentary (*cf.* p. 124). The polar bodies are therefore not only rudimentary cells (Giard, '76), but may further be regarded as *abortive eggs* — a view first put forward by Mark in 1881, and ultimately adopted by nearly all investigators.[1] The evidence is steadily accumulating that reduction is accomplished by two maturation-divisions throughout the animal kingdom, even in the unicellular forms; though in certain Infusoria an additional division occurs, while in some other Protozoa only one maturation-division has thus far been made out. Among plants, also, two maturation-

---

[1] The parallel was first clearly pointed out by Platner in 1889, and was brilliantly demonstrated by Oscar Hertwig in the following year.

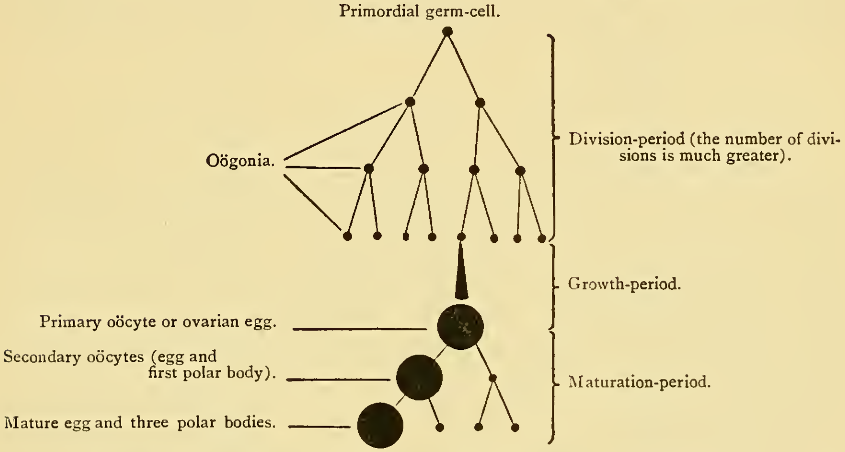
Primordial germ-cell.
Oögonia.
Division-period (the number of divisions is much greater).
Growth-period.
Primary oöcyte or ovarian egg.
Secondary oöcytes (egg and first polar body).
Maturation-period.
Mature egg and three polar bodies.

Fig. 115. — Diagram showing the genesis of the egg. [After BOVERI.]

---

[1] A beautiful confirmation of this view is given by Francottes's ('97) observations on a turbellarian, *Prostheceræus.* The first polar body is here often abnormally large, all gradations having been observed from the normal size up to cells nearly as large as the egg itself. *Such polar bodies are occasionally fertilized* and develop into small gastrulas, first forming a single polar body like the second polar body of the egg. Here, therefore, two of the four cells are exceptionally capable of development. It may be added that Fol long ago observed the penetration of the small polar bodies by spermatozoa in the echinoderms; and this has been more recently observed by Kostanecki in mollusks.

divisions occur in all the higher forms (Muscineæ, pteridophytes, and phanerogams), and in some, at least, of the lower ones. Here, however, the phenomena are complicated by the fact that the two divisions do not as a rule give rise directly to the four sexual germ-cells, but to four asexual spores which undergo additional divisions before the definitive germ-cells are produced. In the flowering plants there are only a few such divisions, which give rise to structures within the pollen-tube or embryo-sac. In the archegoniate cryptogams, on the other hand, each spore gives rise, by repeated divisions, to a "sexual generation" (prothallium, etc.) that intervenes between the process of reduction and that of fertilization. The following account deals primarily with reduction in animals, the plants being afterward considered.

1. *Reduction in the Female. Formation of the Polar Bodies*

As described in Chapter III., the egg arises by the division of cells descended from the primordial egg-cells of the maternal organism, and these may be differentiated from the somatic cells at a very early period, sometimes even in the cleavage-stages. As development proceeds, each primordial cell gives rise, by division of the usual mitotic type, to a number of descendants known as *oögonia* (Fig. 115), which are the immediate predecessors of the ovarian egg. At a certain period these cease to divide. Each of them then grows to form an ovarian egg, its nucleus enlarging to form the germinal vesicle, its cytoplasm becoming more or less laden with food-matters (yolk or deutoplasm), while egg-membranes may be formed around it. The ovum may now be termed the *oöcyte* (Boveri) or ovarian egg.

In this condition the egg-cell remains until near the time of fertilization, when the process of maturation proper — *i.e.* the formation of the polar bodies — takes place. In some cases, *e.g.* in the sea-urchin, the polar bodies are formed before fertilization, while the egg is still in the ovary. More commonly, as in annelids, gasteropods, nematodes, they are not formed until after the spermatozoön has made its entrance; while in a few cases one polar body may be formed before fertilization and one afterward, as in the lamprey-eel, the frog, and *Amphioxus*.[1] In all these cases the essential phenomena are the same. Two minute cells are formed, one after the other, near the upper or animal pole of the ovum (Figs. 97, 116); and in many cases the first of these divides into two as the second is formed (Fig. 89).

A group of four cells thus arises, namely, the mature egg, which gives rise to the embryo, and three small cells or polar bodies which take no part in the further development, are discarded, and soon die without further change. The egg-nucleus is now ready for union with the sperm-nucleus.

---

[1] *Cf.* p. 189.

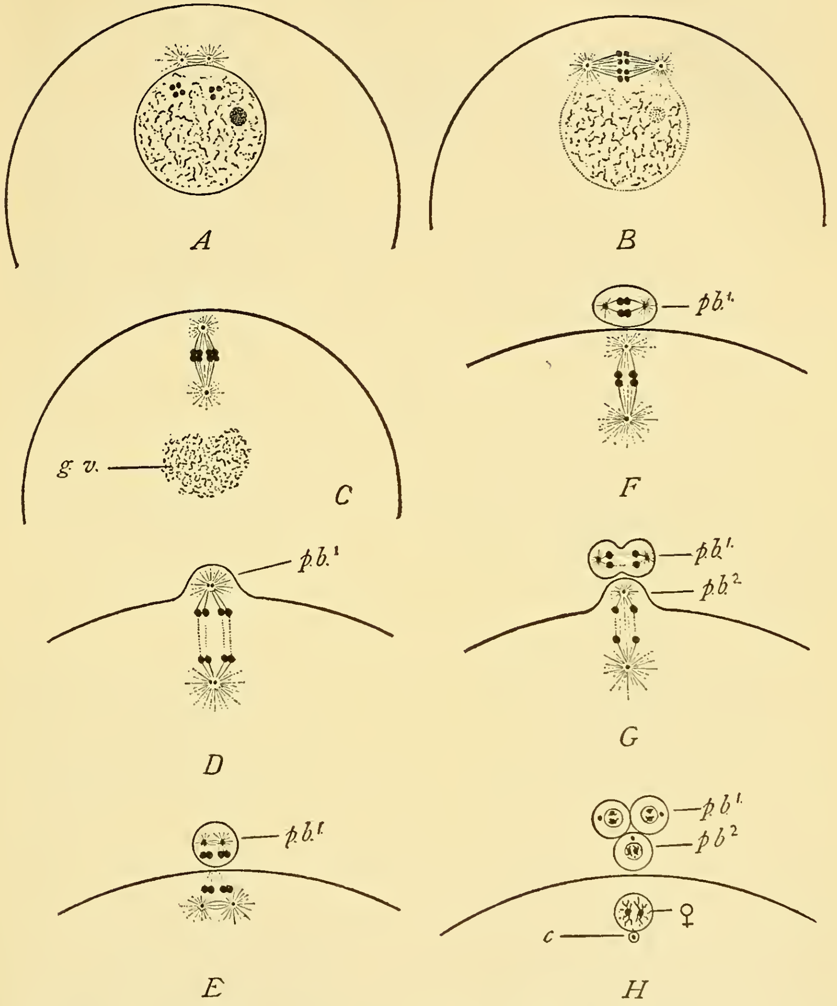

Fig. 116. — Diagrams showing the essential facts in the maturation of the egg. The somatic number of chromosomes is supposed to be four.

A. Initial phase; two tetrads have been formed in the germinal vesicle. *B*. The two tetrads have been drawn up about the spindle to form the equatorial plate of the first polar mitotic figure. *C*. The mitotic figure has rotated into position, leaving the remains of the germinal vesicle at *g.v.* *D*. Formation of the first polar body; each tetrad divides into two dyads. *E*. First polar body formed; two dyads in it and in the egg. *F*. Preparation for the second division. *G*. Second polar body forming and the first dividing; each dyad divides into two single chromosomes. *H*. Final result; three polar bodies and the egg-nucleus (♀), each containing two single chromosomes (half the somatic number); *c*. the egg-centrosome which now degenerates and is lost.

A study of the nucleus during these changes brings out the following facts. During the multiplication of the oögonia the number of chromosomes is the same as that occurring in the division of the somatic cells, and the same number enters into the formation of the chromatic reticulum of the germinal vesicle. During the formation of the polar bodies this number becomes reduced to one-half, the nucleus of each polar body and the egg-nucleus receiving the reduced number. In some manner, therefore, the formation of the polar bodies is connected with the process by which the reduction is effected. The precise nature of this process is, however, a matter which has been certainly determined in only a few cases.

We need not here consider the history of opinion on this subject further than to point out that the early observers, such as Purkinje, Von Baer, Bischoff, had no real understanding of the process and believed the germinal vesicle to disappear at the time of fertilization. To Bütschli ('76), Hertwig, and Giard ('76, '77) we owe the discovery that the formation of the polar bodies is through *mitotic division*, the chromosomes of the equatorial plate being derived from the chromatin of the germinal vesicle.[1] In the formation of the first polar body the group of chromosomes splits into two daughter-groups, and this process is immediately repeated in the formation of the second *without an intervening reticular resting stage.* The egg-nucleus therefore receives, like each of the polar bodies, one-fourth of the *mass* of chromatin derived from the germinal vesicle.

But although the formation of the polar bodies was thus shown to be a process of true cell-division, the history of the chromosomes was found to differ in some very important particulars from that of the tissue-cells. The essential facts, which were first carefully studied in *Ascaris* by Van Beneden ('83, '87), and especially by Boveri ('87, 1), are in a typical case as follows (Figs. 116, 117): As the egg prepares for the formation of the first polar body, the chromatin of the germinal vesicle groups itself in a number of masses, each of which splits up into a group of four bodies united by linin-threads to form a "quadruple group" or tetrad (Vierergruppe). *The number of tetrads is always one-half the usual number of chromosomes.* Thus in *Ascaris* (*megalocephala, bivalens*) the germinal vesicle gives rise to two tetrads, the normal number of chromosomes in the earlier divisions being four; in the mole-cricket there are six tetrads, the somatic number of chromosomes being twelve; in *Cyclops* the respective numbers are twelve and twenty-four (one of the most frequent cases); while in *Artemia* there are eighty-four tetrads and one hundred and sixty-eight somatic chromosomes — the highest number thus far accurately counted. As the first polar body forms, each of the tetrads is halved to form two double groups, or *dyads*, one of which remains in the egg

---

[1] The early accounts asserting the disappearance of the germinal vesicle were based on the fact that in many cases only a small fraction of the chromatic network gives rise to chromosomes, the remainder disintegrating and being scattered through the yolk.

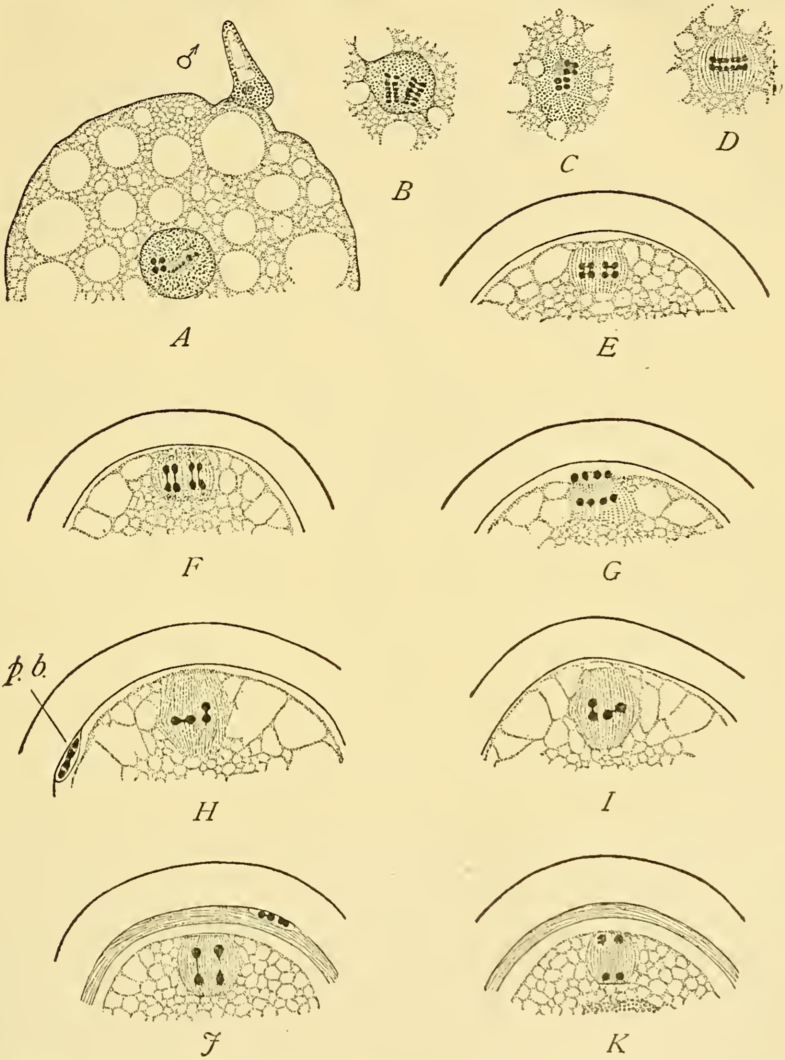

Fig. 117. — Formation of the polar bodies in *Ascaris megalocephala*, var. *bivalens*. [BOVERI.]

A. The egg with the spermatozoön just entering at ♂; the germinal vesicle contains two rod-shaped tetrads (only one clearly shown), the number of chromosomes in earlier divisions having been four. *B*. The tetrads seen in profile. *C*. The same in end view. *D*. First spindle forming (in this case inside the germinal vesicle). *E*. First polar spindle. *F*. The tetrads dividing. *G*. First polar body formed, containing, like the egg, two dyads. *H*. *I*. The dyads rotating into position for the second division. *J*. The dyads dividing. *K*. Each dyad has divided into two single chromosomes, completing the reduction. (For later stages see Fig. 90.)

while the other passes into the polar body. Both the egg and the first polar body therefore receive each a number of dyads equal to one-half the usual number of chromosomes. The egg now proceeds at once to the formation of the second polar body without previous reconstruction of the nucleus. Each dyad is halved to form two single chromosomes, one of which, again, remains in the egg while its sister passes into the polar body. Both the egg and the second polar body accordingly receive two single chromosomes (one-half the usual number), each of which is one-fourth of an original tetrad group. From the two remaining in the egg a reticular nucleus, much smaller than the original germinal vesicle, is now formed.[1]

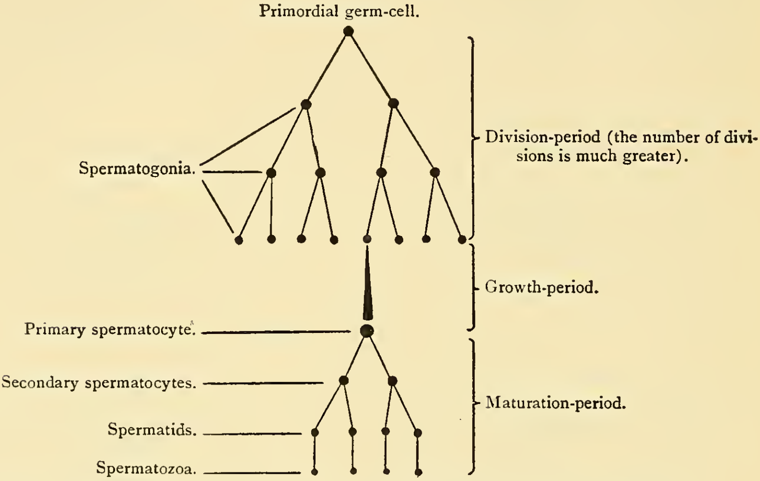

Fig. 118. — Diagram showing the genesis of the spermatozoön. [After BOVERI.]

Essentially similar facts have now been determined in a considerable number of animals, though, as we shall presently see, tetrad-formation is not of universal occurrence, nor is it always of the same type. For the moment we need only point out that the numerical reduction of chromatin-*masses* takes place before the polar bodies are actually formed, through processes which determine the number of tetrads within the germinal vesicle. The numerical reduction is therefore determined in the grandmother-cell of the egg. The actual divisions by which the polar bodies are formed merely distribute the elements of the tetrads.

---

[1] It is nearly certain that the division of the first polar body (which, however, may be omitted) is analogous to that by which the second is formed, *i.e.* each of the dyads is similarly halved. *Cf.* Griffin, '99.

2. *Reduction in the Male. Spermatogenesis*

The researches of Platner ('89), Boveri, and especially of Oscar Hertwig ('90, 1) have demonstrated that reduction takes place in the male in a manner almost precisely parallel to that occurring in the female. Platner first suggested ('89) that the formation of the polar bodies is directly comparable to the last two divisions of the sperm mother-cells (spermatocytes). In the following year Boveri reached the same result in *Ascaris*, stating his conclusion that reduction in the male must take place in the "grandmother-cell of the spermatozoön, just as in the female it takes place in the grandmother-cell of the egg," and that the egg-formation and sperm-formation really agree down to the smallest detail ('90, p. 64). Later in the same year appeared Oscar Hertwig's splendid work on the spermatogenesis of *Ascaris*, which established this conclusion in the most striking manner. Like the ova, the spermatozoa are descended from primordial germ-cells which by mitotic division give rise to the *spermatogonia* from which the spermatozoa are ultimately formed (Fig. 118). Like the oögonia, the spermatogonia continue for a time to divide with the usual (somatic) number of chromosomes, *i.e.* four in *Ascaris megalocephala bivalens*. Ceasing for a time to divide, they now enlarge considerably to form *spermatocytes*, each of which is morphologically equivalent to an unripe ovarian ovum, or *oöcyte*. Each spermatocyte finally divides twice in rapid succession, giving rise first to two daughter-spermatocytes and then to four *spermatids*, each of which is directly converted into a single spermatozoön. *The history of the chromatin in these two divisions is exactly parallel to that in the formation of the polar bodies* (Figs. 119, 120). From the chromatin of the spermatocyte are formed a number of tetrads equal to one-half the usual number of chromosomes. Each tetrad is halved at the first division to form two dyads which pass into the respective daughter-spermatocytes. At the ensuing division, which occurs without the previous formation of a resting reticular nucleus, each dyad is halved to form two single chromosomes which enter the respective spermatids (ultimately spermatozoa). From each spermatocyte, therefore, arise four spermatozoa, and each sperm-nucleus receives half the usual number of single chromosomes. The parallel with the egg-reduction is complete.

These facts leave no doubt that the spermatocyte is the morphological equivalent of the oöcyte or immature ovarian egg, and that the group of four spermatozoa to which it gives rise is equivalent to the ripe egg plus the three polar bodies. Hertwig was thus led to the following beautifully clear and simple conclusion: "The polar bodies are abortive eggs which are formed by a final process of division from the egg-mother-cell (oöcyte) in the same manner as the spermatozoa are formed from the sperm-mother-cell (spermatocyte). But while in the latter case the products of the division are all used as functional spermatozoa, in the former case one of the products of the egg-mother-cell becomes the egg, appropriating to itself the entire mass of the yolk at the cost of the others which persist in rudimentary form as the polar bodies."[1]

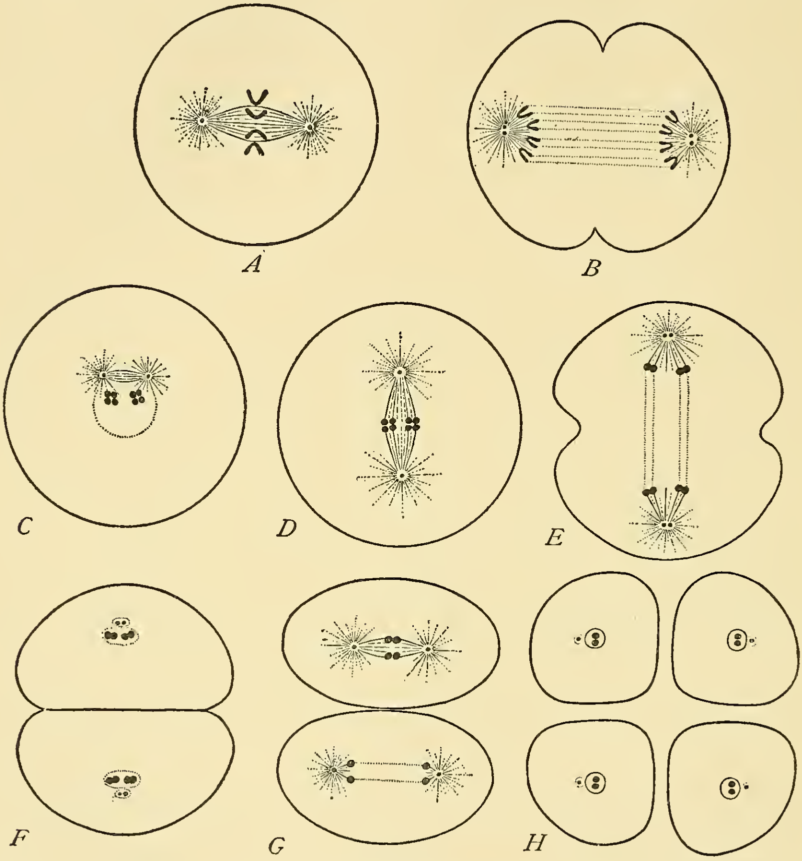

Fig. 119. — Diagrams showing the essential facts of reduction in the male. The somatic number of chromosomes is supposed to be four.

A. B. Division of one of the spermatogonia, showing the full number (four) of chromosomes. *C.* Primary spermatocyte preparing for division; the chromatin forms two tetrads. *D. E. F.* First division to form two secondary spermatocytes each of which receives two dyads. *G. H.* Division of the two secondary spermatocytes to form four spermatids. Each of the latter receives two single chromosomes and a centrosome which passes into the middle-piece of the spermatozoön.

---

[1] '90, I, p. 126.

3. *Weismann's Interpretation of Reduction*

Up to this point the facts are clear and intelligible. Before coming to closer quarters with them it will be useful to make a digression in order to consider some of the theoretical aspects of reduction; though the reader must be warned that this will lead us into very uncertain ground traversed by a labyrinth of conflicting hypotheses from which no exit has yet been discovered.

The process of reduction is very obviously a provision to hold constant the number of chromosomes characteristic of the species; for if it did not occur, the number would be doubled in each succeeding generation through union of the germ-cells.[1] A number of writers have contented themselves with this simple interpretation, Oscar Hertwig, for example, regarding reduction as "merely a process to prevent a summation through fertilization of the nuclear mass and of the chromatic elements."[2] A moment's reflection reveals the entire inadequacy of such an explanation. As far as the chromatin-mass is concerned, it does not agree with the facts; for in reduction with tetrad-formation the chromatin-mass is reduced not to one-half, but to one-fourth. That reduction must mean more than mere mass-reduction is moreover proved by the fact that the bulk of the nucleus may enormously increase or decrease at different periods in the same cell, irrespective of the number of chromosomes. The real problem is why the number of chromosomes should be held constant. The deeper meaning of the phenomena was first seriously considered by Weismann in his essays of 1885 and 1887; and, although his conclusions were of a highly speculative character, they nevertheless gave so great a stimulus to the study of the entire problem that his views deserve special attention. Weismann's interpretation was based on a remarkable paper published by Wilhelm Roux in 1883,[2] in which are

---

[1] Of the many earlier attempts to interpret the meaning of the polar bodies, we need only consider at this point the very interesting suggestion of Minot ('77), afterward adopted by Van Beneden ('83), that the ordinary cell is hermaphrodite, and that maturation is for the purpose of producing a unisexual germ-cell by dividing the mother-cell into its sexual constituents, or "genoblasts." Thus, the male element is removed from the egg *in the polar bodies*, leaving the mature egg a female. In like manner he believed the female element to be cast out during spermatogenesis (in the "Sertoli cells"), thus rendering the spermatozoa male. By the union of the germ-cells in fertilization, the male and female elements are brought together so that the fertilized egg or oösperm is again hermaphrodite or neuter. This ingenious view was independently advocated by Van Beneden in his great work on *Ascaris* ('83). A fatal objection to it, on which both Strasburger and Weismann have insisted, lies in the fact that male as well as female qualities are transmitted by the egg-cell, while the sperm-cell also transmits female qualities. The germ-cells are therefore non-sexual. The researches of many observers show, moreover, that all of the four spermatids derived from a spermatocyte become functional spermatozoa. Minot's hypothesis must, therefore, in my opinion, be abandoned.

Balfour doubtless approximated more nearly to the truth when he said, "In the formation of the polar cells part of the constituents of the germinal vesicle, which are requisite for its functions as a complete and independent nucleus, is removed to make room for the supply of the necessary parts to it again by the spermatic nucleus" ('80, p. 62). He fell, however, into the same error as Minot and Van Beneden in characterizing the germ-nuclei as "male" and "female"; and, as shown at pages 194, 353, it has been found that a single germ-nucleus is able to carry out development of an embryo without union with another.

[2] '90, 1, p. 112. *Cf.* Hartog, '91, p. 57.

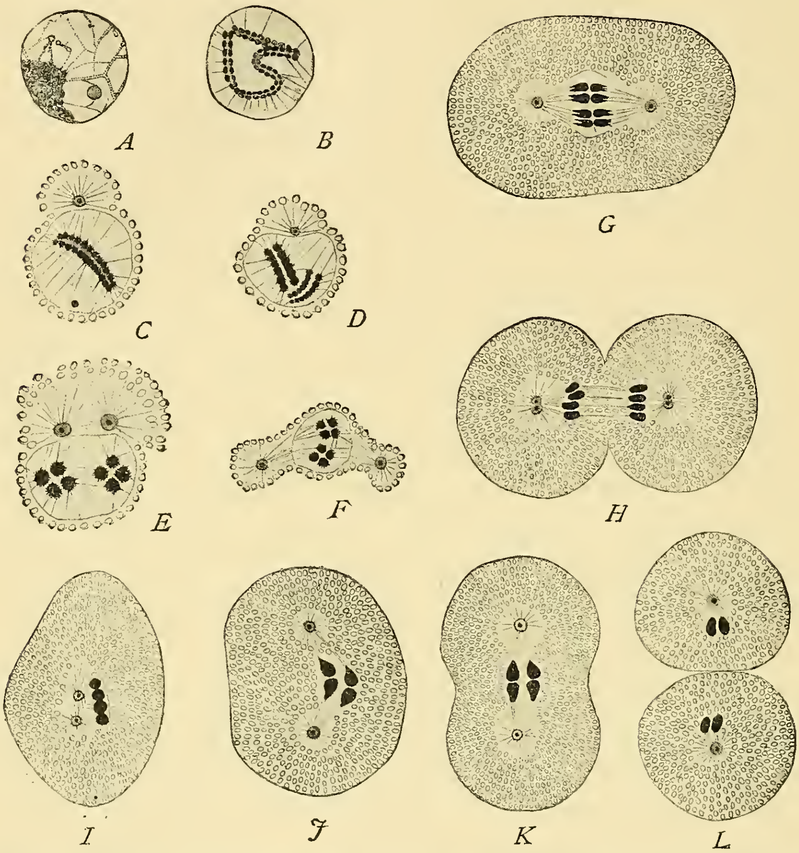

Fig. 120. — Reduction in the spermatogenesis of *Ascaris megalocephala*, var. *bivalens*. [BRAUER.][1]

A–G. Successive stages in the division of the primary spermatocyte. The original reticulum undergoes a very early division of the chromatin-granules which then form a doubly split spireme-thread, *B*. This shortens (*C*), and breaks in two to form the two tetrads (*D* in profile, *E* viewed endwise). *F. G. H.* First division to form two secondary spermatocytes, each receiving two dyads. *I.* Secondary spermatocyte. *J. K.* The same dividing. *L.* Two resulting spermatids, each with two single chromosomes and a centrosome.

---

[1] For division of the spermatogonia see Fig. 55; for the corresponding phenomena in var. *univalens* see Fig. 148.

[2] *Über die Bedeutung der Kerntheilungsfiguren.*

developed certain ideas which afterward formed the foundation of Weismann's whole theory of inheritance and development. Roux argued that the facts of mitosis are only explicable under the assumption that chromatin is not a uniform and homogeneous substance, but differs qualitatively in different regions of the nucleus; that the collection of the chromatin into a thread and its accurate division into two halves is meaningless unless the chromatin in different regions of the thread represents different *qualities* which are to be divided and distributed to the daughter-cells according to some definite law. He urged that if the chromatin were qualitatively the same throughout the nucleus, direct division would be as efficacious as indirect, and the complicated apparatus of mitosis would be superfluous. Roux and Weismann, each in his own way, subsequently elaborated this conception to a complete theory of inheritance and development, but at this point we may confine our attention to the views of Weismann. The starting-point of his theory is the hypothesis of De Vries that the chromatin is a congeries or colony of invisible self-propagating vital units or *biophores* somewhat like Darwin's "gemmules" (p. 12), each of which has the power of determining the development of a particular quality. Weismann conceives these units as aggregated to form units of a higher order known as "determinants," which in turn are grouped to form "ids," each of which, for reasons that need not here be specified,[1] is assumed to possess the complete architecture of the germ-plasm characteristic of the species. The "ids" finally, which are identified with the visible chromatin-granules, are arranged in linear series to form "idants" or chromosomes. It is assumed further that the "ids" differ slightly in a manner corresponding with the individual variations of the species, each chromosome therefore being a particular group of slightly different germ-plasms and differing qualitatively from all the others.

We come now to the essence of Weismann's interpretation. The end of fertilization is to produce new combinations of variations by the mixture of different ids. Since, however, their number, like that of the chromosomes which they form, is doubled by the union of two germ-nuclei, an infinite complexity of the chromatin would soon arise did not a periodic reduction occur. Assuming, then, that the "ancestral germ-plasms" (ids) are arranged in a linear series in the spireme-thread or the chromosomes derived from it, Weismann ventured the prediction ('87) that two kinds of mitosis would be found to occur. The first of these is characterized by a longitudinal splitting of the thread, as in ordinary cell-division, "by means of which all the ancestral germ-plasms are equally distributed in each of the daughter-nuclei after having been divided into halves." This form of division, which he called *equal division* (Aequationstheilung), was then a known fact. The second form, at that time a purely theoretical postulate, he assumed to be of such a character that each daughter-nucleus should receive only half the number of ancestral germ-plasms possessed by the mother-nucleus. This he termed a *reducing division* (Reduktionstheilung), and suggested that this might be effected either by a *transverse* division of the chromosomes, or by the elimination of entire chromosomes without division.[1] By either method the number of "ids" would be reduced; and Weismann argued that such reducing divisions must be involved in the formation of the polar bodies, and in the parallel phenomena of spermatogenesis.

---

[1] *Cf.* the Germ-plasm, p. 60.

The fulfilment of Weismann's prediction is one of the most interesting results of recent cytological research. It has been demonstrated, in a manner which seems to be incontrovertible, that the reducing divisions postulated by Weismann actually occur, though not precisely in the manner conceived by him. Unfortunately for the general theory, however, transverse divisions have been certainly determined in only a few types, while in others, of which *Ascaris* is the best-known example, the facts thus far known seem clearly opposed to the assumption. On the whole, the evidence of reducing divisions, *i.e.* such as involve a transverse and not a longitudinal division of the chromatin-thread, has steadily increased; but it remains quite an open question whether they have the significance attributed to them by Weismann.

B. Origin of the Tetrads

1. *General Sketch*

In considering the origin of the tetrads or their equivalents, it should be borne in mind that true tetrad-formation, as described above, has only been certainly observed in a few groups (most clearly in the nematodes and arthropods). But even in cases where the chromatin does not condense into actual tetrads these bodies are represented by chromosomes in the form of rings, crosses, and the like, which are closely similar, and doubtless equivalent, to those from which actual tetrads arise, and present us with the same problems. With a few apparent exceptions, described hereafter, the tetrads of their equivalents always arise by a double division of a single primary chromatin-rod or mass. Nearly all observers agree further that the number of primary rods at their first appearance in the germinal vesicle or in the spermatocyte-nucleus is *one-half the usual number of chromosomes*, and that this numerical reduction is due to the fact that the spireme-thread segments into one-half the usual number of pieces. Apparently, however, there are two radically different types of tetrad-formation as follows.

---

[1] Essay VI., p. 375.

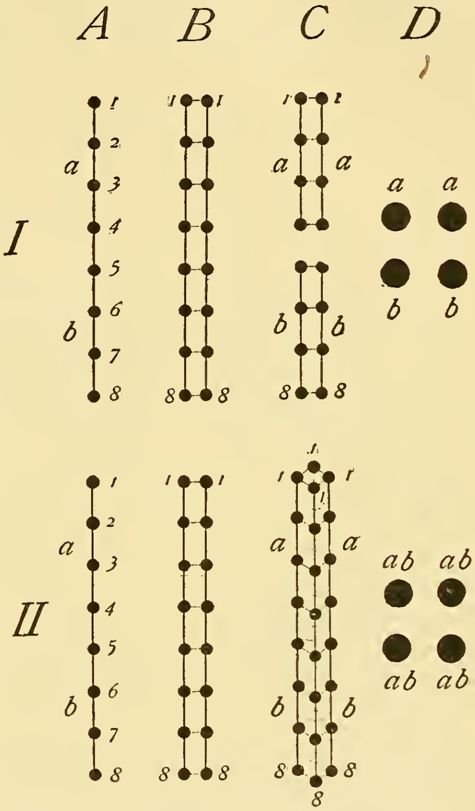

Fig. 121. — Diagrams of tetrad-formation; I, with one transverse and one longitudinal division (copepod type); II, with two longitudinal divisions (*Ascaris* type). *A–D*, successive stages; chromatin-granules numbered from 1 to 8. The two types diverge at *C*. In *D* the granules of each constituent of the tetrad fuse to form a homogeneous sphere.

In the first type the tetrad arises by *one longitudinal and one transverse division of each primary chromatin-rod*, the latter effecting the reduction demanded by Weismann's hypothesis (Fig. 121, I). To give the usual graphic representation, let us, for the sake of discussion, assume the somatic number of chromosomes to be four, designating the spireme-thread as *a b c d*, each letter representing a chromosome, each of which we may in turn assume to consist of a series of four granules or "ids" (Fig. 121). In ordinary mitosis the spireme would segment into $a - b - c - d$, which then would divide lengthwise to form pairs of identical sister chromosomes $\frac{a}{a} - \frac{b}{b} - \frac{c}{c} - \frac{d}{d}$. To form the tetrad, on the other hand, the spireme first segments into two rods *ab* and *cd*, each of which, in view of its subsequent history, may be regarded as bivalent, representing two chromosomes united end to end (Vom Rath, Rückert, Häcker). Each of these divides once longitudinally, giving the identical pairs or dyads $\frac{ab}{ab} - \frac{cd}{cd}$, and once transversely, giving the tetrads $\frac{a}{a}\left|\frac{b}{b} - \frac{c}{c}\right|\frac{d}{d}$. Inspection of Fig. 121, I, shows that through the second or transverse division, each member of the tetrad receives only half the number of ids contained in the original segment. This number, four, is the same as that assumed for a single chromosome; and, since each of the two tetrads contributes one chromosome to the germ-cell, the latter receives but half the usual number both of chromosomes and of ids. This mode of tetrad-formation has been most clearly demonstrated in insects and copepods, and an equivalent process occurs also in mollusks, annelids, turbellarians, and some other animals, as described beyond.

In the second type, illustrated especially by *Ascaris*, the tetrad is apparently formed by *two longitudinal divisions* of each primary chromatin-rod, and no reducing division occurs. If, therefore, we adopt the same terminology as before, we have first *ab* and *cd*, then $\frac{ab}{ab} - \frac{cd}{cd}$, and finally $\frac{ab}{ab}\Big|\frac{ab}{ab} - \frac{cd}{cd}\Big|\frac{cd}{cd}$, by two longitudinal divisions. In this case, according to Brauer's careful studies, each chromatin-granule ("id") divides at each longitudinal division of the primary rod. The four chromosomes of the tetrad are therefore exactly equivalent, being derived from the same region of the spireme-thread, and containing the undiminished number of "ids" (Fig. 121, II).

The contradiction may be stated in a different way. In the first type of tetrad formation, the number both of granules and of chromosomes is first *doubled* (*i.e.* in the assumed case, through the formation of two tetrads, each consisting of four chromosomes, or eight in all), and then reduced to half that number by the two successive maturation-divisions. In the second type, on the other hand, the number of chromosomes is likewise doubled, but that of the granules is *quadrupled*, so that, although in both types the two maturation-divisions reduce the number of *chromosomes* to one-half, only in the first type do they reduce the number of granules or "ids," as Weismann's hypothesis demands. We must therefore distinguish sharply between the reduction of the chromosomes and that of the "ids." The former is primarily effected by the segmentation of the primary spireme-thread, or the resolution of the nuclear reticulum, into one-half the usual number of segments (*i.e.* the "pseudo-reduction" of Rückert); and *here the real secret of the reduction of the chromosomes lies.* The reduction of the "ids," if they have any real existence, is a distinct, and as yet unsolved, question.

2. *Detailed Evidence*

We may now consider some of the phenomena in detail, though the limits of this work will only allow the consideration of a few typical cases.

(*a*) *Tetrad-formation with one Longitudinal and one Transverse Division.* — In many of the cases of this type the tetrads arise from ring-shaped bodies which are analogous to the ring-shaped chromosomes occurring in heterotypical mitosis (p. 86). First observed by Henking ('91) in *Pyrrhocoris*, tetrad-origin of this type has since been found in other insects by Vom Rath, Toyama, Paulmier, and others, in copepods by Rückert, Häcker, and Vom Rath, in pteridophytes by Calkins and Osterhout, in the onion, *Allium*, by Ishikawa, and in various other forms where their history has been less clearly made out. The genesis of the ring was first determined by Vom Rath in the mole cricket (*Gryllotalpa*, '92), and has been thoroughly elucidated by the later work of Rückert ('94), Häcker ('95, 1), and Paulmier ('99). All these observers have reached the same conclusion; namely, that the ring arises by the longitudinal splitting of a primary chromatin-rod, the two halves remaining united by their ends, and opening out to form a ring. The ring-formation is, in fact, a form of heterotypical mitosis (p. 86). The breaking of the ring into four parts involves, first, the separation of these two halves (corresponding with the original longitudinal split), and second, the *transverse* division of each half, the latter being the reducing division of Weismann. The number of primary rods, from which the rings arise, is one-half the somatic number. Hence each of them is conceived by Vom Rath, Häcker, and Rückert as bivalent or double; *i.e.* as representing two chromosomes united end to end. This appears with the greatest clearness in the spermatogenesis of *Gryllotalpa* (Fig. 122). Here

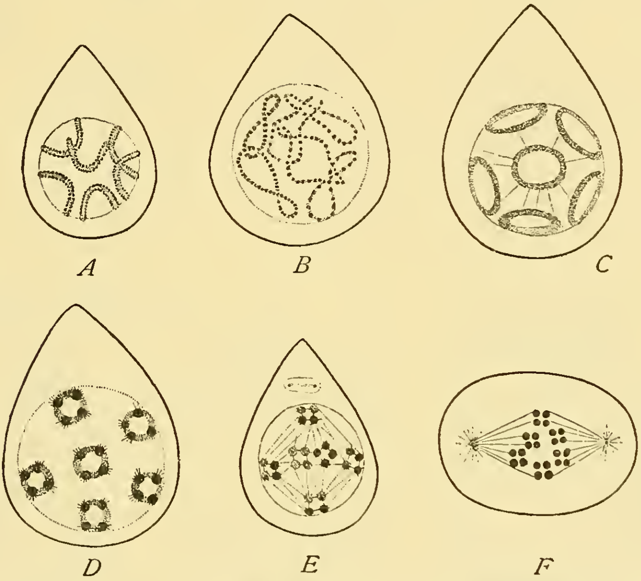

Fig. 122. — Origin of the tetrads by ring-formation in the spermatogenesis of the mole-cricket *Gryllotalpa*. [Vom Rath.]

A. Primary spermatocyte, containing six double rods, each of which represents two chromosomes united end to end and longitudinally split except at the free ends. *B. C.* Opening out of the double rods to form rings. *D.* Concentration of the rings. *E.* The rings broken up into tetrads. *F.* First division-figure established.

the spireme-thread splits lengthwise before its segmentation into rods. It then divides transversely to form six double rods (half the usual number of chromosomes), which open out to form six closed rings. These become small and thick, break each into four parts, and thus give rise to six typical tetrads. An essentially similar account of the ring-formation is given by Vom Rath in *Euchæta* and *Calanus*, and by Rückert in *Heterocope* and *Diaptomus*.

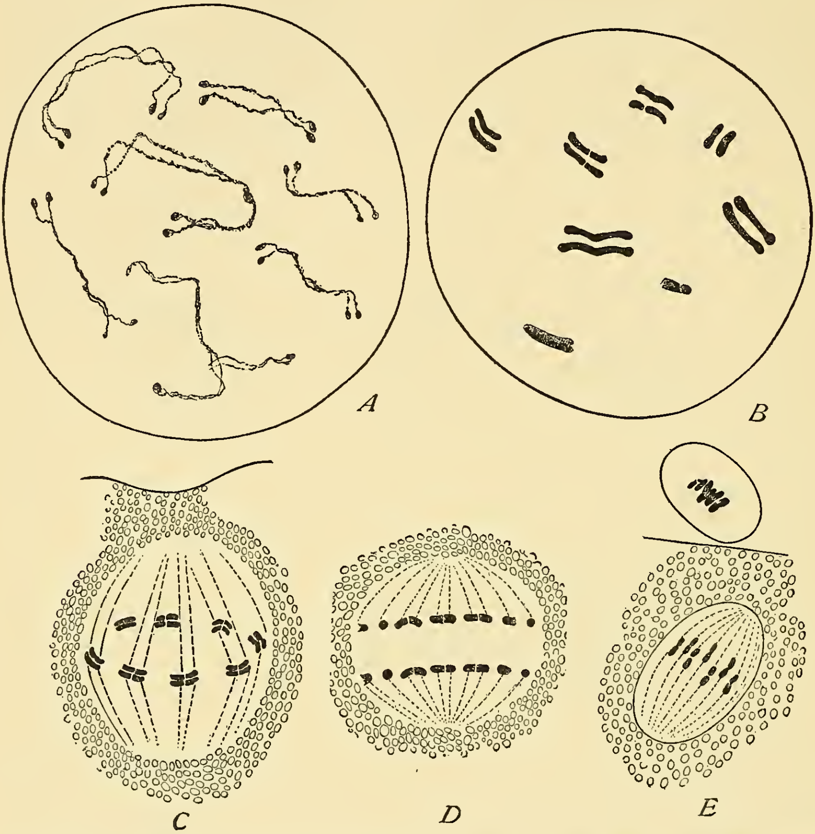

Fig. 123. — Formation of the tetrads and polar bodies in *Cyclops*, slightly schematic. (The full number of tetrads is not shown.) [RÜCKERT.]

A. Germinal vesicle containing eight longitudinally split chromatin-rods (half the somatic number). *B.* Shortening of the rods; transverse division (to form the tetrads) in progress. *C.* Position of the tetrads in the first polar spindle, the longitudinal split horizontal. *D.* Anaphase; longitudinal divisions of the tetrads. *E.* The first polar body formed; second polar spindle with the eight dyads in position for the ensuing division, which will be a *transverse* or reducing division.

That the foregoing interpretation of the rings is correct, is beautifully demonstrated by the observations of Häcker, and especially of

Rückert, on a number of other copepods (*Cyclops*, *Canthocamptus*), in which rings are not formed, since the splitting of the primary chromatin-rods is complete. The origin of the tetrads has here been traced with especial care in *Cyclops strenuus*, by Rückert ('94), whose observations, confirmed by Häcker, are quite as convincing as those of Brauer on *Ascaris*, though they led to a diametrically opposite result.

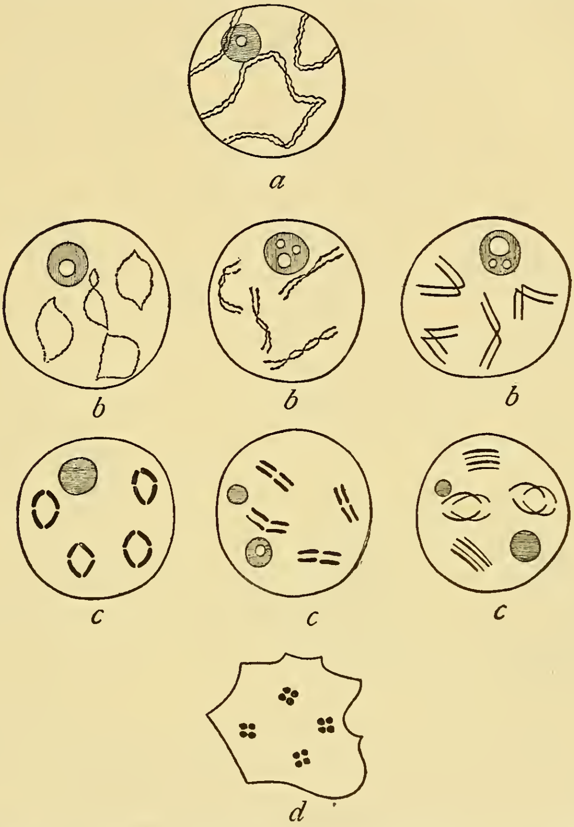

Fig. 124. — Diagrams of various modes of tetrad-formation. [HÄCKER.]

a. Common starting-point, a double spireme-thread in the germinal vesicle; *d.* common result, the typical tetrads; *b. c.* intermediate stages: at the left the ring-formation (as in *Diaptomus*, *Gryllotalpa*, *Heterocope*); middle series, complete splitting of the rods (as in *Cyclops* according to Rückert, and in *Canthocamptus*); at the right by breaking of the V-shaped rods (as in *Cyclops strenuus*, according to Häcker.

The normal number of chromosomes is here twenty-two. In the germinal vesicle arise eleven threads, which split lengthwise (Fig. 123), and finally shorten to form double rods, manifestly equivalent to the closed rings of *Diaptomus*. Each of these now segments *transversely* to form a tetrad group, and the eleven tetrads then place themselves in the equator of the spindle for the first polar body (Fig. 123, *C*), in such a manner that the *longitudinal split* is transverse to the axis of the spindle. As the polar body is formed, the longitudinal halves of the tetrad separate, and the formation of the first polar body is thus demonstrated to be an "equal division" in Weismann's sense. The eleven dyads remaining in the eggs now rotate (as in *Ascaris*), so that the transverse division lies in the equatorial plane, and are halved during the formation of the second polar body. The division is accordingly a "reducing division," which leaves eleven single chromosomes in the egg. Paulmier's work on *Anasa* and other Hemiptera ('99) gives the same result as the above in regard to the origin of the tetrads (Figs. 126, 127). The process is, however, slightly complicated by the fact that no continuous spireme-thread is formed, while the rings are often bent or twisted and never open out to a

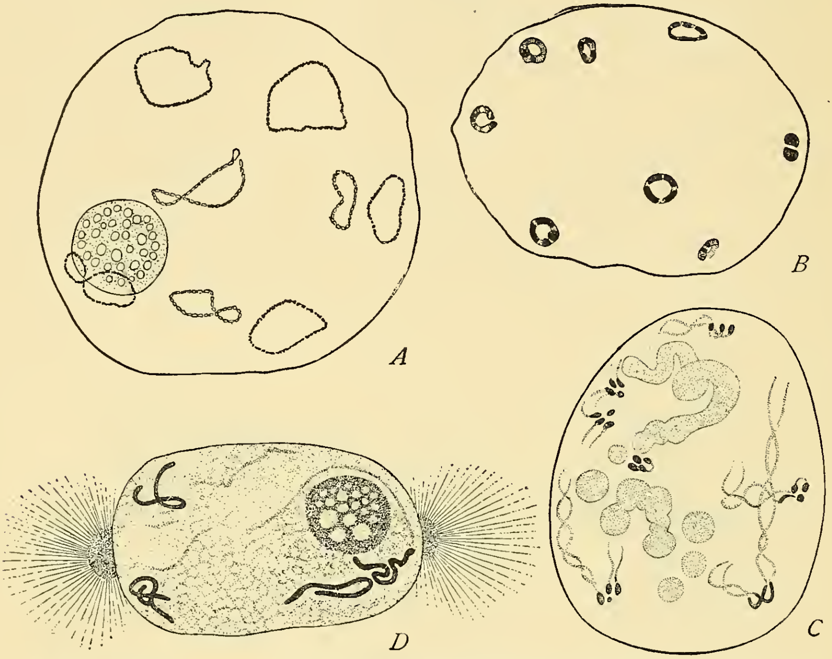

Fig. 125. — Germinal vesicles of various eggs, showing chromosomes, tetrads, and nucleoli.

A. A copepod (*Heterocope*) showing eight of the sixteen ring-shaped tetrads and the nucleolus. [RÜCKERT.]

B. Later stage of the same, condensation and segmentation of the rings. [RÜCKERT.]

C. "*Cyclops strenuus*," illustrating Häcker's account of the tetrad-formation from elongate double rods; a group of "accessory nucleoli." [HÄCKER.]

D. Germinal vesicle of an annelid (*Ophryotrocha*) showing nucleolus and four chromosomes. [KORSCHELT.]

circular form. They finally condense into true tetrads which are successively divided into dyads and monads by the two divisions; but it is an interesting fact that the order of division occurring in the copepods appears here to be reversed, the first division being the transverse and the second the longitudinal one — a result agreeing with Henking's earlier conclusion in the case of *Pyrrochoris*. Osterhout ('97) and Calkins ('97) independently discovered tetrads in the vascular cryptogams (*Equisetum*, *Pteris*), and the last-named observer finds that in *Pteris* they may arise either from rings, as in *Gryllotalpa* or *Heterocope*, or from double rods as in *Cyclops*, the halves in the latter case being either parallel or forming a cross. This longitudinal split, occurring in the spireme, is followed by a transverse division by which the tetrad is formed. Tetrads having an essentially similar mode of origin are also described by Atkinson ('99) in *Arisæma*, and tetrad-formation is nearly approached in *Allium* according to Ishikawa ('99).[1] These cases are considered at page 263.

Résumé. In all the foregoing cases the tetrads arise from a spireme which splits lengthwise, segments into one-half the somatic number of rods (each longitudinally divided) and each of the latter divides transversely to form the tetrad. When the ends of the daughter-chromosomes resulting from the longitudinal split remain united (as in insects) ring-forms result, and the earlier phases of tetrad-formation are thus identical with those of heterotypical mitosis. When the split is complete, so that the ends remain free, double rods result; while, if the daughter-chromosomes remain temporarily united at the middle or at the end, X-, Y-, and V-shaped figures may arise. In all these forms tetrad-formation is completed by the complete separation of the daughter-rods, the transverse division of each in the middle, and the condensation of the four resulting bodies into a quadruple mass. As will be shown in Section C (p. 258) the transverse division is in many forms delayed until after separation of the longitudinal halves. In such cases no actual tetrads are formed, though the result is the same.

(*b*) *Second Type. Tetrad-formation with two Longitudinal Divisions.* — The only accurately known case of this type is *Ascaris*, the object in which tetrads were first discovered by Van Beneden in 1883. Carnoy ('86, 2) reached the conclusion that the tetrads in some other nematodes (*Ophiostomum*, *Ascaris clavata*, *A. lumbricoides*) arose by a double longitudinal splitting of the primary chromatin-rods.

---

[1] Vom Rath ('93, '59) has endeavoured to show that a process involving the formation of true tetrads occurs in the salamander and the frog, but the later and more accurate studies of Meves ('96) seem to leave little doubt that this was an error, and that the tetrads observed in these forms are not of normal occurrence, as Flemming ('87) had earlier concluded. *Cf.* p. 259.

In the first of his classical cell-studies Boveri ('87, 1) reached the same result through a careful study of *Ascaris megalocephala*, showing that each tetrad appears in the germinal vesicle in the form of four parallel rods, each consisting of a row of chromatin-granules (Fig. 117, *A–C*). He believed these rods to arise by the double longitudinal splitting of a single primary chromatin-rod, each cleavage being a preparation for one of the polar bodies. In his opinion, therefore, the formation of the polar bodies differs from ordinary mitosis only in the fact that the chromosomes split very early, and not once, but twice, in preparation for two rapidly succeeding divisions without an intervening resting period. He supported this view by further observations in 1890 on the polar bodies of *Sagitta* and several gasteropods, in which he again determined, as he believed, that the tetrads

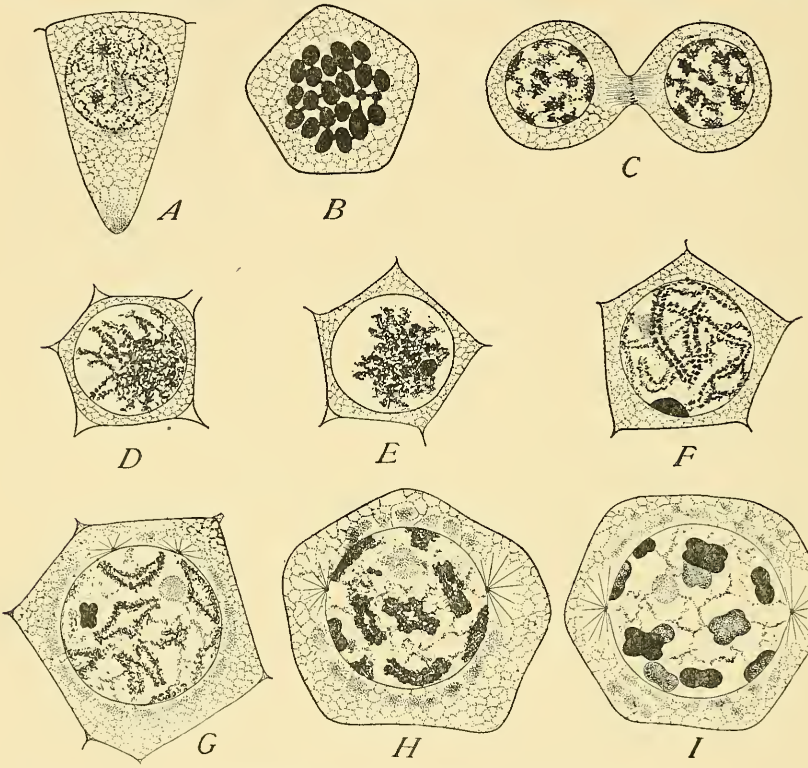

Fig. 126. — Tetrad-formation in an insect, *Anasa*. [PAULMIER.]

A. Resting spermatogonium with single plasmosome and two chromatin-nucleoli. *B.* Equatorial plate of dividing spermatogonium; twenty large and two small chromosomes. *C.* Final spermatogonium-division. *D–I.* Prophases of first maturation-division. *D. E.* Synapsis, with single chromatin-nucleolus. *F.* Segmented split spireme. *G. H.* Formation of the tetrad-rings. *H. I.* Concentration of the rings to form tetrads.

arose by double longitudinal splitting. An essentially similar view of the tetrads was taken by Hertwig in 1890, in the spermatogenesis of *Ascaris*, though he could not support this conclusion by very convincing evidence. In 1893, finally, Brauer made a most thorough and apparently exhaustive study of their origin in the spermatogenesis of *Ascaris*, which seemed to leave no doubt of the correctness of Boveri's result. Every step in the origin of the tetrads from the reticulum of the resting spermatocytes was traced with the most painstaking care. In the early prophases of the first division the nuclear reticulum breaks up more or less completely into granules, which become in part aggregated in a mass at one side of the nucleus ("synapsis," p. 276), from which delicate threads extend through the remaining nuclear space (Fig. 120, *A*). Even at this period the granules of the threads are divided into four parts. As the process proceeds the chromatin resolves itself into a single spireme-thread, consisting of four parallel rows of granules, which break in two to form the two tetrads (var. *bivalens*), or is directly converted into a single tetrad (var. *univalens*) (Fig. 120). From these observations Brauer concludes that each tetrad arises from a rod, doubly split lengthwise by a process initiated at a very early period through the

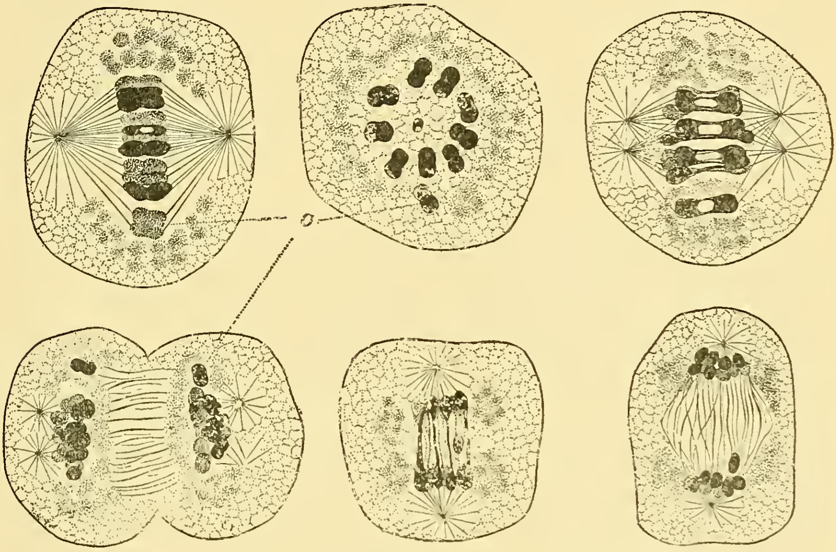

Fig. 127. — Maturation-divisions in an insect, *Anasa*. [PAULMIER.]

A. Primary spermatocyte in metaphase. *B*. Equatorial plate, showing ten large tetrads and one small one; "odd chromosome" at *o*. *C*. Separation of the dyads. *D*. Telophase, which is also a prophase of the second division. *E*. Secondary spermatocyte; division of the dyads; small dyad shown undivided. *F*. Final anaphase; small dyad near the lower chromosome-group. (The figures are numbered from left to right. For later states, see Fig. 82.)

double fission of the chromatin-granules. If this be correct, there can be no reduction in Weismann's sense; for the four products of each primary chromatin-granule are equally distributed among the four daughter-cells. A similar conclusion, based on much more incomplete evidence, was reached by Brauer ('92) in the phyllopod *Branchipus*.

Brauer's evidently conscientious figures very strongly sustain his conclusion, which, reinforced by the earlier work of Hertwig and Boveri, has until now seemed to rest upon an unassailable basis. The recent work of Sabaschnikoff ('97) nevertheless raises the possibility of a different interpretation. Brauer himself justly urges that the essence of the process lies in the double fission of the chromatin-granules to which the formation of chromosomes is secondary.[1] Everything, therefore, turns on the manner in which the quadruple granules arise; and Sabaschnikoff's work gives some ground for the view that they may arise, not by a double fission, but in some other way.

According to this author there is a period (in the oögenesis) at which the nuclear threads wholly disappear, the entire chromatin being broken up into granules. From this state the granules emerge in quadruple form to arrange themselves in the doubly split spireme exactly as Brauer describes; and a few observations are given (regarding the size and arrangement of the granules) which suggest the possibility that the quadruple granules may arise by the *conjugation* either of four separate granules or of two pairs of double granules. Since there is ground for the view that tetrads may arise by the conjugation of chromosomes (see following section), there is no *a priori* objection to such a conclusion. Could it be sustained, the maturation-divisions of *Ascaris* would in fact involve a true reduction in Weismann's sense; for despite the fact that the chromosomes are only longitudinally divided, the four longitudinal constituents of each tetrad would not be equivalent with respect to the granules, and it is the reduction of the latter ("ids") that forms the essence of Weismann's hypothesis (p. 245). Another consideration, suggested to me by Professor T. H. Morgan, opens still another possibility, which seems well worthy of test by further research. As already stated (p. 88), the long chromosomes of *Ascaris* are plurivalent, since in all but the germ-cells each breaks up into a much larger number of smaller chromosomes (Fig. 73, p. 148). If, therefore, the latter correspond to the chromosomes of other forms in which tetrads occur (*e.g. Cyclops* or *Artemia*), the so-called "tetrad" of *Ascaris* is a compound body; and the true process of reduction must be sought in the origin of the smaller elements of which it is composed, which are, perhaps, directly comparable with Sabaschnikoff's "granules." Until the questions thus opened have been further studied, the case for *Ascaris* must remain open; and it is perhaps worth suggesting that a new point of view may here be found for further study also of reduction in the vertebrates.[2]

---

[1] *Cf.* p. 113.

[2] Bodies closely resembling tetrads are sometimes formed in mitosis, where no reduction should occur. Thus, R. Hertwig ('95) has observed tetrads in the first cleavage-spindle of echinoderm-eggs after treatment with dilute poisons (p. 306). Klinckowström figures them in the *second* polar spindle of *Prosthecerœus* eggs, while Moore ('95) describes in the elasmobranchs small ring-shaped chromosomes, not only in the first but also in the *second* spermatocyte-divisions, concluding that no reduction occurs in either division.

(*c*) *The Formation of Tetrads by Conjugation.* — A considerable number of observers have maintained that reduction may be effected by the union or conjugation of chromosomes that were previously separate. This view agrees in principle with that of Rückert, Häcker, and Vom Rath; for the bivalent chromosomes assumed by these authors may be conceived as two conjugated chromosomes. It seems to be confirmed by the observations of Born and Fick on Amphibia and those of Rückert on selachians (*Pristiurus*); for in all these cases the number of chromatin-masses at the time the first polar body is formed is but half the number observed in younger stages of the germinal vesicle. In *Pristiurus* there are at first thirty-six double segments in the germinal vesicle. At a later period these give rise to a close spireme, which then becomes more open, and is found to form a double thread segmented into eighteen double segments; *i.e.* the reduced number. In this case, therefore, the preliminary pseudo-reduction is almost certainly effected by the union of the original thirty-six double chromosomes, two by two. The most specific accounts of such a mode of origin have, however, been given by Calkins (earthworm) and Wilcox (grasshopper). The latter author asserts ('95) that in *Caloptenus* the spireme of the first spermatocyte gives rise without longitudinal division to twenty-four chromosomes (double the somatic number). These then become associated in pairs, and still later the twelve pairs conjugate two and two to form six tetrads. There is, therefore, no longitudinal splitting of the chromosomes. The *a priori* improbability of such a conclusion is increased by the studies of Paulmier on the Hemiptera, which demonstrate the occurrence of a longitudinal division in a number of these forms and confirm the original studies of Vom Rath on *Gryllotalpa*.[1]

The second case, which is perhaps better founded, is that of the earthworm (*Lumbricus terrestris*), as described by Calkins ('95, 2), whose work was done under my own direction. Calkins finds that the spireme splits longitudinally and then divides transversely into 32 double segments. These then unite, two by two, to form 16 tetrads. The 32 primary double segments therefore represent chromosomes of the normal number that have split longitudinally, *i.e.* $\frac{a}{a} - \frac{b}{b}$, etc., and the formula for a tetrad is $\frac{a}{a}\Big|\frac{b}{b}$ or $\frac{a}{a}\Big|\frac{x}{x}$. Such a tetrad, therefore, agrees as to its composition with the formulas of Häcker, Vom Rath, and Rückert, and agrees in mode of origin with the process described by Rückert in the eggs of *Pristiurus*. While these observations are not absolutely conclusive, they nevertheless rest on strong evidence, and they do not stand in actual contradiction of what is known in the copepods and vertebrates. The possibility of such a mode of origin in other forms must, I think, be held open.

---

[1] Montgomery, who has denied the occurrence of a longitudinal division in *Pentatoma* ('98, 1), has subsequently found such a division in the nearly related if not identical genus *Euchistis* ('99).

Under the same category must be placed Korschelt's unique results in the egg-reduction of the annelid *Ophryotrocha* ('95), which are very difficult to reconcile with anything known in other forms. The typical somatic number of chromosomes is here four. The *same number* of chromosomes appear in the germinal vesicle (Fig. 125, *D*). They are at first single, then double by a longitudinal split, but afterward single again by a reunion of the halves. The four chromosomes group themselves in a single tetrad, two passing into the first polar body, while two remain in the egg, but meanwhile each of them again splits into two. Of the four chromosomes thus left in the egg two are passed out into the second polar body, while the two remaining in the egg give rise to the germ-nucleus. From this it follows that the formation of the *first* polar body is a reducing division — a result which agrees with the earlier conclusions of Henking on *Pyrrochoris*, and with those of Paulmier on the Hemiptera.

C. Reduction without Tetrad-formation

As already stated (p. 246), the formation of actual tetrads is of relatively rare occurrence, being thus far certainly known only in the arthropods, nematodes, and some annelids. In the greater number of cases the two divisions of the primary chromatin-masses (*i.e.* of the primary oöcyte or spermatocyte) are separated by a considerable interval, during which the first maturation cell-division takes place or is initiated, and hence no actual tetrads are formed. This obviously differs only in degree from tetrad-formation, the latter occurring only when the two divisions are simultaneous or occur in rapid succession.

In the cases now to be considered the length of the pause between the maturation-divisions varies considerably, and in some forms (vertebrates, flowering plants) it is so prolonged that the nucleus is partially reconstructed. In all, or nearly all, these cases the *first maturation-division is of the heterotypical form*, the chromosomes having the form of rings and arising by a process that agrees in most of its features with that leading to tetrad-formation. There is here, however, exactly the same contradiction of results as in the case of tetrad-formation described at page 247, and a bewildering confusion of the subject still exists. In brief, it may be stated that most observers of reduction of this type in the lower animals (flat-worms, annelids, mollusks) have found one transverse and one longitudinal division; most of those who have studied the vertebrates find two longitudinal divisions; while opinion regarding the plants is still divided.

(*a*) *Animals.* — In the gephyrean *Thalassema* and the mollusk *Zirphæa* (Figs. 128–130) Griffin ('99) finds that the rings, arising as described above, place themselves in the equator of the spindle with the longitudinal division in the equatorial plane. They are then drawn out toward the spindle-poles from the middle point, first assuming the form of a double cross, then of elongated ellipses, and finally break into two daughter-U's or -V's. The first division is therefore longitudinal. During the late anaphase the V's break at the apex, the two limbs come close together, so as to give the deceptive appearance of a longitudinal split, and are separated by the second division (following immediately upon the first without intervening resting stage). The latter is therefore a transverse division (Fig. 130). An essentially similar result, though less completely worked out, is independently reached by Bolles Lee ('97) in *Helix;* by Klinckowström ('97) in the turbellarian *Prosthecerœus;* and by Francotte ('97) and Van der Stricht ('98, 1) in *Thysanzoon.* Klinckowström shows that there is much variation in the way in which the rings open out and break apart, though the result is the same in all.

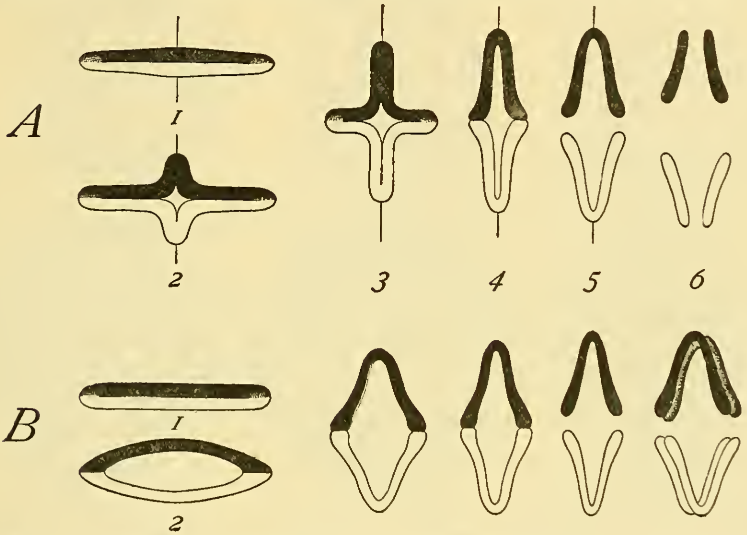

Fig. 128. — Diagrams of reduction in the types represented by *Thalassema* (*A*) and *Salamandra* (*B*). In both the first division is heterotypical. The second division (6) is transverse in the first and longitudinal in the second.

In case of the vertebrates, Flemming ('87) long since described and figured typical tetrads in the salamander, but regarded them as "anomalies." Vom Rath's later conclusion ('93, '95) that they are normal tetrads has not been sustained by the still more recent work of Meves ('96), whose careful studies, together with those of Moore, Lenhossék, and others, thus far give no evidence of tetrad-formation, and seem opposed to the occurrence of reducing divisions in the vertebrates. Meves's work in the main confirms the earlier results of Flemming, except that he shows that, as in so many other animals, only two generations of spermatocytes exist. At the first division the nuclear reticulum resolves itself into twelve (the reduced number) segments, which split lengthwise, the halves remaining united to form elongated rings (Figs. 27, 37). These do not, however, condense into tetrads, but break apart during the first division at the points corresponding with the ends of the united halves. The first division is therefore an equation-division. As the V-shaped halves separate they again split lengthwise (Fig. 131), each of the secondary spermatocytes receiving twelve double V's or dyads. In the telophases and ensuing resting stage, however, all traces of this splitting are lost, the nuclei partially returning to the resting stage, but retaining traces of a spireme-like arrangement (Fig. 131). In the second division twelve double V's reappear, showing a longitudinal division which Flemming and Meves believe to be directly related to that

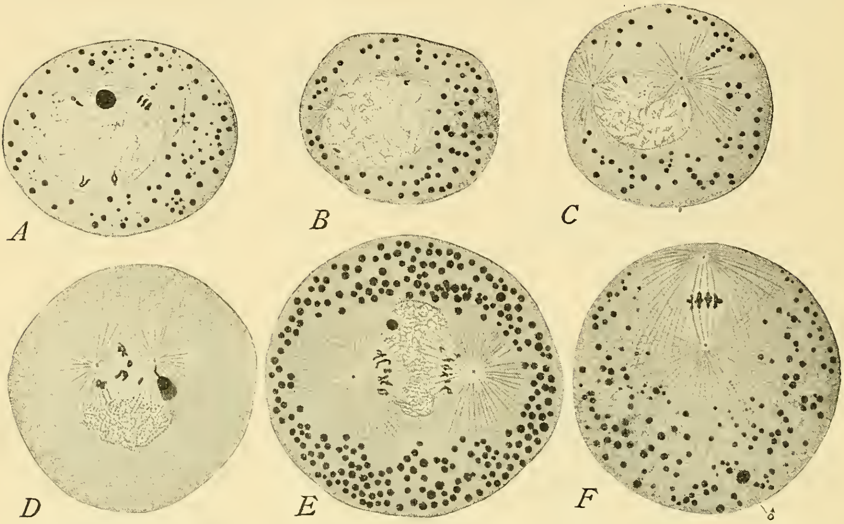

Fig. 129. — Maturation and fertilization in an annelid (armed gephyrean) *Thalassema*. [Griffin.]

A. A few moments after entrance of the spermatozoon, showing accessory asters; tetrads forming. *B.* Early prophase of first polar mitosis with centrosomes. *C.* In-pushing of nuclear wall. *D.* Central spindle established; elimination of nucleolus and nuclear reticulum. *E.* Slightly later stage viewed from above. *F.* First polar spindle established, cross-shaped tetrads, crossing of astral rays; sperm-head at ♂.

seen during the foregoing anaphases. There is therefore no evidence of a transverse division. McGregor ('99) describes a nearly similar process in *Amphiuma*, where the longitudinal division of the daughter-V's is seen with the greatest clearness throughout the anaphases.

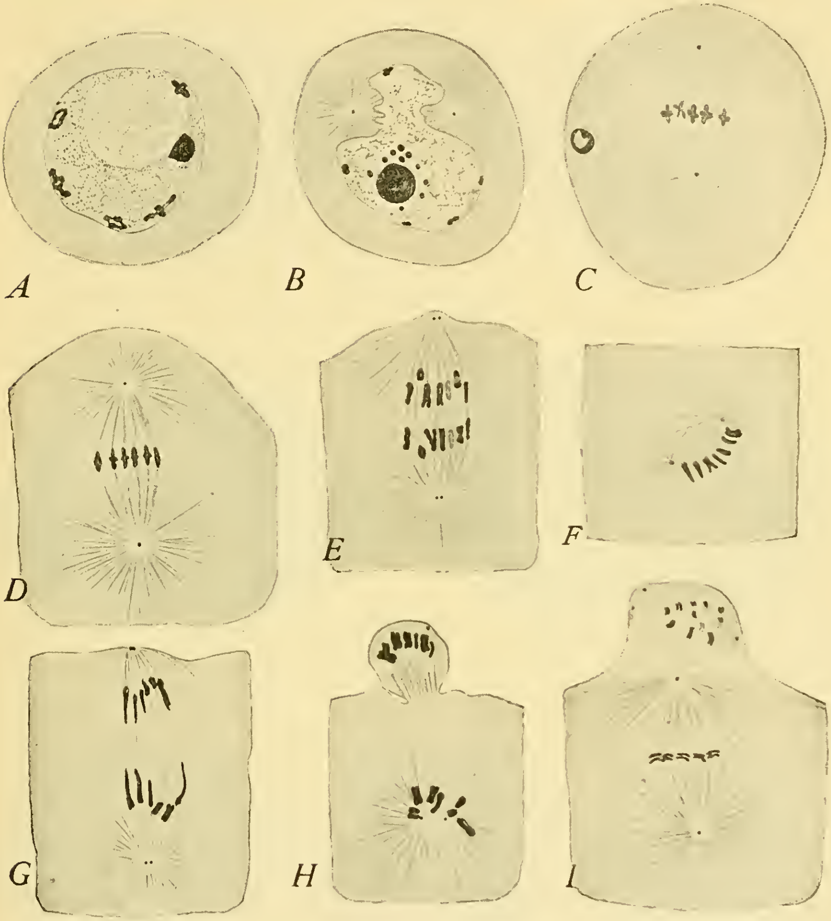

Fig. 130. — Maturation in the lamellibranch *Zirphæa* and in *Thalassema*. [GRIFFIN.]

A–E, *Zirphæa*; *F–I*, *Thalassema*.

A. Unfertilized egg, ring-shaped and cross-shaped chromosomes. *B*. Prophase of first polar mitosis. *C*. First polar spindle; double crosses. *D*. Slightly later stage. *E*. The double crosses have broken apart (equation-division). *G*. Ensuing stage; daughter-V's broken apart at the apex. *H*. Telophase of first, early prophase of second, division; limbs of the V's separate but closely opposed. *F*. Later prophase of second division. *I*. Second polar spindle in metaphase.

The weak point in both the foregoing cases is the fact that all traces of the second longitudinal division are lost during the ensuing resting period; and I do not think that even the observations of Flemming ('97), who has published the fullest evidence in the case, completely establish the occurrence of a subsequent longitudinal division of the chromosomes in the second mitosis. In *Desmognathus*, however, where the resting stage is less complete, Kingsbury ('99) finds the longitudinal split in the persistent chromosomes of the

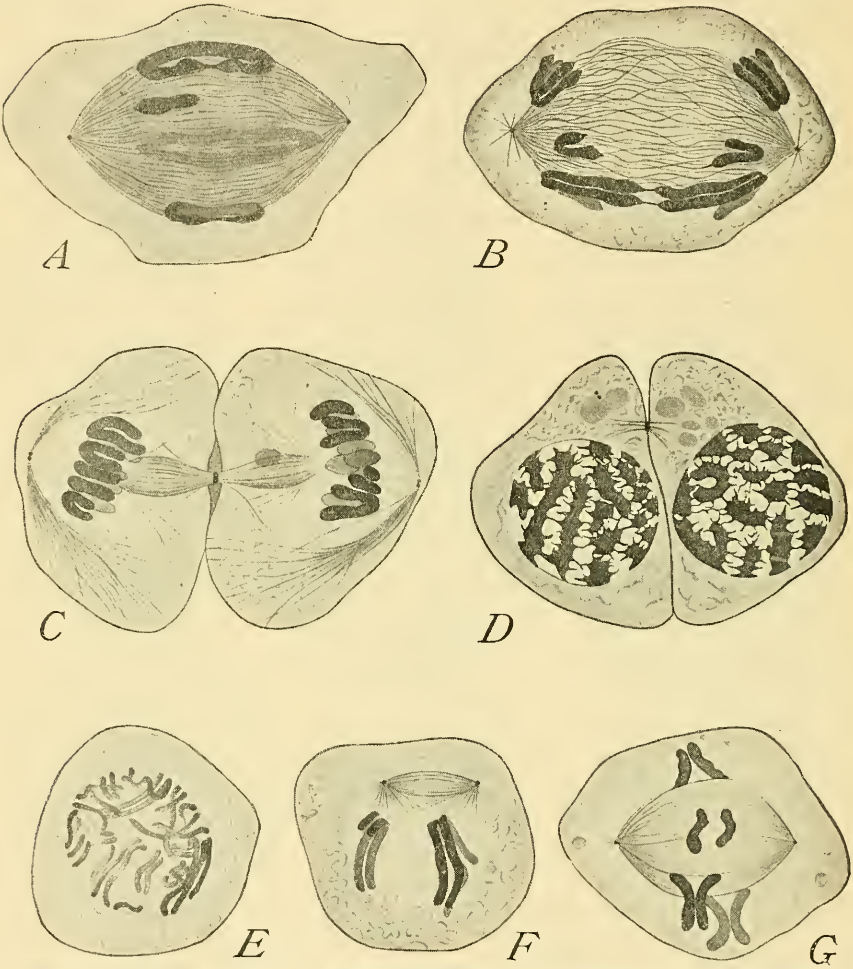

Fig. 131. — (Compare Fig. 27). Maturation-divisions in *Salamandra*. [*E* from FLEMMING, the others from MEVES.]

A. First division in metaphase, showing heterotype rings. *B*. Anaphase; longitudinal splitting of the daughter-loops. *C*. Telophase. *D*. Ensuing pause. *E*. Early prophase of second division with longitudinally divided segmented spireme. *F*. Later prophase. *G*. Metaphase of second division.

pause following the first division; and he believes this to be the same division as that seen during the anaphase. Carnoy and Le Brun ('99) reach the same result in the formation of the polar bodies in *Triton*, though their general account of the heterotypical mitosis differs very considerably from that of other authors, the rings being stated to arise by a double instead of a single longitudinal split. These observers describe the rings of the early anaphase as having almost exactly the same double cross-form as those in *Thalassema* or *Zirphœa* (Griffin, '99), but believe them to arise in a manner nearly in accordance with Strasburger's abandoned view of 1895,[1] and with Guignard's ('98, 2) and Grégoire's ('99) latest results on the flowering plants, the ring being stated to arise by a double longitudinal splitting, as explained at page 265.

In the elasmobranch *Scyllium* Moore ('95) finds twelve (the reduced number) ring-shaped chromosomes at the first division. These closely resemble tetrads; but a resting stage follows, and the second division is likewise stated to be of the heterotypical form. Both divisions are stated to be equation-divisions — a conclusion well supported in case of the first, but so far from clear in the second that a careful reëxamination of the matter is highly desirable.

In mammals the first division is of the heterotypical form (Hermann, '89, Lenhossék, '98), though the rings are much smaller than in the salamander, recalling those seen in arthropods. No true tetrads are, however, formed, and the two divisions are separated by a resting period. The character of the second division is undetermined, though Lenhossék believes it to be heterotypical, like the first.

(*b*) *Plants.* — It is in the flowering plants, where reduction likewise occurs, as a rule, without true tetrad-formation, that the contradiction of results reaches its climax; and it must be said that until further research clears up the present confusion no definite result can be stated. The earlier work of Strasburger and Guignard indicated that no reducing division occurred, the numerical reduction being directly effected by a segmentation of the spireme-thread into half the somatic number of chromosomes. Thus these observers found in the male that the chromosomes suddenly appeared in the reduced number (twelve in the lily, eight in the onion) at the first division of the pollen-mother-cell, and in the female at the first division of the mother-cell of the embryo-sac. The subsequent phenomena differ in a very interesting way from those in animals, owing to the fact that the two maturation-divisions are followed in the female by one and in the male by two or more additional divisions, in both of which the reduced number of chromosomes persists. In the male the two maturation-divisions give rise to four pollen-grains, in the female to the four primary cells of the embryo-sac (Fig. 132); and these two divisions undoubtedly correspond to the two maturation-divisions in animals. In the female, as in the animals, only one of the four resulting cells gives rise to the egg, the other three corresponding to the polar bodies in the animal egg, though they here continue to divide, and thus form a rudimentary prothallium.[1] The first-men-

---

[1] *Cf.* p. 269.

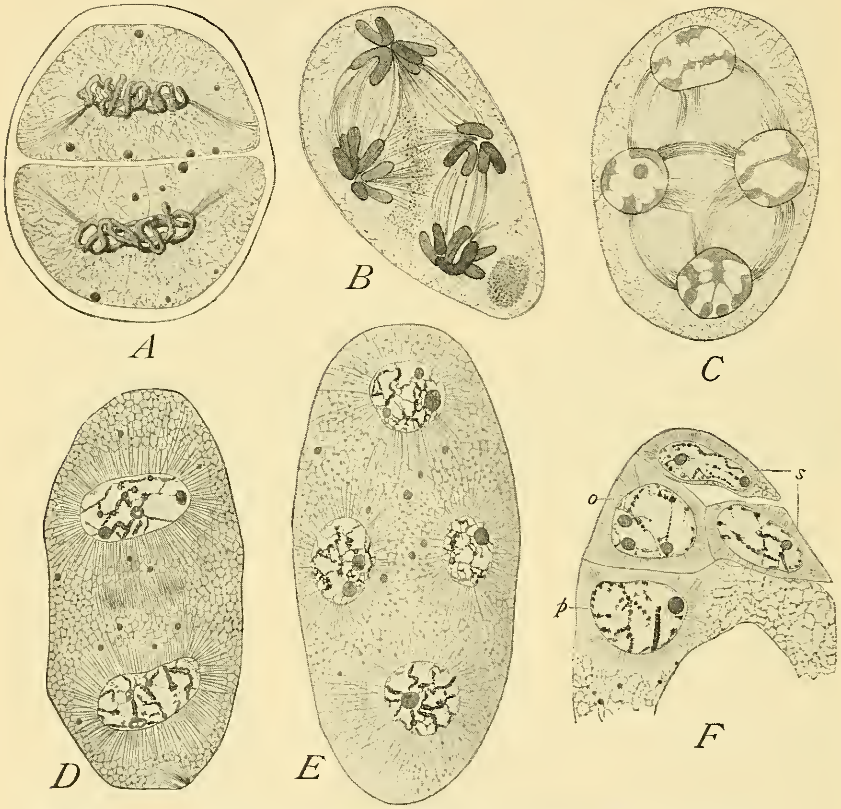

Fig. 132. — General view of the maturation-divisions in flowering plants. [MOTTIER.]

A–C, in the male; *D–F*, in the female. *A*. The two secondary spermatocytes (pollen-mother-cells) just after the first division (*Lilium*). *B*. Final anaphase of second division (*Podophyllum*). *C*. Resulting telophase, which by division of the cytoplasmic mass produces four pollen-grains. *D*. Embryo-sac after completion of the first nuclear division (*Lilium*). *E*. The same after the second division. *F*. The upper four cells resulting from the third division (*cf.* Fig. 106) : *o*, ovum; *p*, upper polar cell; *s*, synergidæ. (For further details, see Figs. 133, 134.)

---

[1] Of these three cells one divides to form the "synergidæ," the other two divide to form three "antipodal cells" (which like the synergidæ finally degenerate) and a "lower polar cell." The latter sooner or later conjugates with the "upper polar cell" (the sister-cell of the egg) to form the "secondary embryo-sac-nucleus," by the division of which the endosperm-cells arise. Of the whole group of eight cells thus arising only the egg contributes

tioned cell, however, does not directly become the egg, but divides once, one of the products being the egg and the other the "upper polar cell" (Fig. 132, *F*), which contributes to the endosperm-formation (see footnote, and compare page 218).

In the male the two maturation-divisions are in the angiosperms followed by two others, one of which separates a "vegetative" from a "generative" cell, while the second divides the generative nucleus into two definite germ-nuclei. In the gymnosperms more than two such additional divisions take place. In these later divisions, both in the male and in the female (with the exception noted in the footnote below), the reduced number persists, and the principal interest centres in the first two or maturation-divisions. Strasburger and Guignard found in *Lilium* that while both these divisions differed in many respects from the mitosis of ordinary vegetative cells, neither involved a transverse or reducing division, the chromosomes undergoing a longitudinal splitting for each of the maturation-divisions. Further investigations by Farmer ('93), Belajeff ('94), Dixon ('96), Sargant ('96, '97), and others, showed that the first division is often of the heterotypical form, the daughter-chromosomes in the late-metaphase having the form of two V's united by their bases (<>). Despite the complication of these figures, due to torsion and other modifications, their resemblance to the ring-shaped bodies observed in the first maturation-division of so many animals is unmistakable, as was first clearly pointed out by Farmer and Moore ('95).

Botanists have differed, and still differ, widely in their interpretation both of the origin and subsequent history of these bodies upon which the question of reduction turns. According to Strasburger's ('95) first account their origin has nothing in common with that of the tetrad-rings, since they were described as arising by a *double* longitudinal splitting of a primary rod, the halves then separating first from one end along one of the division-planes, and then from the other end along the other plane, meanwhile opening out to form a ring such as is shown in Fig. 133. (This process, somewhat difficult to understand from a description, will be understood from the diagram, Fig. 135, *E–I*.) The four elements of the ring are then distributed without further division by the two ensuing maturation-divisions; and the process, except for the peculiar opening out of the ring, is

---

to the morphological formation of the embryo. It is a highly interesting fact that the number of chromosomes shown in the division of the lower of the two nuclei (*i.e.* the mother-nucleus of the antipodal cells and lower polar-cell) formed at the first division of the embryo-sac-nucleus is inconstant, varying in the lily from 12, 16, 20, to 24 (Guignard, '91, 1), in which respect they contrast with the descendants (egg, synergidæ) of the upper nucleus, which always show the reduced number (Mottier, '97, 1), *i.e.* in *Lilium* twelve. This exception only emphasizes the rule of the constancy of the chromosome-number in general; for these cells are destined to speedy degeneration.

essentially in agreement with the facts described in *Ascaris*, and involves no reduction-division. Essentially the same result is reached by Guignard ('98) in his latest paper on *Naias*, and by Gregoire ('99) in the Liliaceæ.

Strasburger twice shifted ground in rapid succession. First ('97, 2), with Mottier ('97, 1), he somewhat doubtfully adopted a view agreeing essentially with the interpretation of Vom Rath, Rückert, etc. (p. 247). The primary rods split once, and bend into a V, the branches of which often come close together, and may be twisted on themselves, thus giving the appearance of the second longitudinal split described in Strasburger's paper of 1895. The two halves of the split U then separate, opening out from the apex, to form the <>-figure. In the

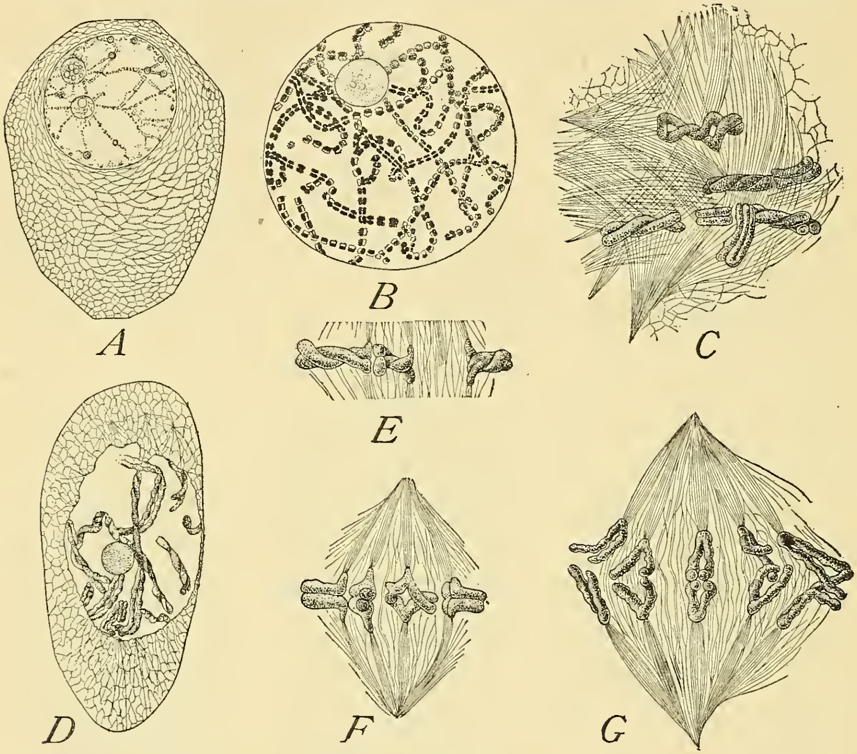

Fig. 133.—The first maturation-division in flowering plants. [*F*, STRASBURGER and MOTTIER; the others from MOTTIER.]

A. Mother-cell of the embryo-sac in *Lilium;* early prophase of first division; chromatin-threads already longitudinally divided. *B*. Slightly later stage (split spireme) in the nucleus of the pollen-mother-cell. *C*. A slightly later prophase (pollen-mother-cell, *Podophyllum*) with twisted split spireme. *D*. Earlier prophase (*Lilium*, female); split twisted chromosomes. *E*. Equatorial plate (*Lilium*, male). *F*. First maturation-spindle (*Fritillaria*, male). *G*. Divergence of the daughter-chromosomes (*Lilium*, male).

second division the limbs of the daughter-V's again come close together, remaining, however, united at one end, where they were believed finally to break apart during the second division. The latter was, therefore, regarded as a true reduction-division, the apparent longitudinal split being merely the plane along which the halves of the V come into contact (Fig. 134, *C*, *D*).

The two accounts just given represent two extremes, the first agreeing essentially with *Ascaris*, the second with the copepods or insects. When we compare them with others, we encounter a truly bewildering confusion. Strasburger and Mottier ('97) themselves soon abandoned their acceptance of the reducing division, returning to the conclusion that in both sexes (*Lilium*, *Podophyllum*) both divisions involve a longitudinal splitting of the chromosomes (Figs. 133, 134). In the first division the longitudinally split spireme segments into twelve double rods, which bend at the middle to form double V's, with closely approximated halves. Becoming attached to the spindle by the apex, the limbs of each separate to form a <> -figure. At telophase the daughter-V's shorten, thicken, and join together to form a daughter-spireme consisting of a single contorted thread. *This splits lengthwise throughout its whole extent*, and then segments into double chromosomes, the halves of which separate at the second division (Fig. 135, *L–M*). The latter, therefore, like the first, involves no reducing division. This result agrees in substance with the slightly earlier work of Dixon ('96) and of Miss Sargant ('96, '97), whose account of the origin of the <> -figure of the first division differs, however, in some interesting details. It is also in harmony with the general results of Farmer and Moore ('95), of Grégoire ('99), and of Guignard ('98), who, however, describes the first division nearly in accordance with Strasburger's account of 1895, as stated above. On the other hand, Ishikawa (pollen-mother-cells of *Allium*, '97) and especially Belajeff (pollen-mother-cells of *Iris*, '98) conclude that the second division is a true transverse or reducing division.[1] Ishikawa described the first division as being nearly similar to the ring-formation in copepods, the four elements of the ring being often so condensed as nearly to resemble an actual tetrad. In the early anaphases the daughter-V's break at the apex; and, although in the later anaphases the limbs reunite, Ishikawa is inclined to regard the transverse division as being a preparation for the second mitosis. Belajeff's earlier work ('94) on *Lilium* gave an indecisive result, though one on the whole favourable to a reducing division. In his latest paper, however ('98, 1), Belajeff takes more positive ground, stating that after the examination of a large number of forms he has found in the pollen-mother-cells of *Iris* a much more favourable object of investigation than *Lilium*, *Fritillaria*, and the other forms on which most of the work thus far has been done, and one in which the second division takes place with "admirable clearness"; he also gives interesting additional details of the first division in this and other forms. In the first division the spireme splits lengthwise, and then breaks into chromosomes, which assume the shape of a V, Y, or X (Fig. 135, *N–Q*). The two limbs of these bodies do not, as might be supposed, represent sister-chromosomes (resulting from the longitudinal division of the spireme) attached by one end or at the middle, since each X, Y, or V is double, consisting of two similar superimposed halves. Belajeff, therefore, regards these figures as longitudinally divided bivalent chromosomes, having the value of tetrads, each limb being a longitudinally split single chromosome. The double V's, Y's, and X's take up a position with the apex (or one end of the X) attached to the spindle, and the longitudinal division in the equatorial plane. The halves then progressively diverge from the

---

[1] Schaffner ('97, 2) reaches exactly the reverse result in *Lilium philadelphicum*, *i.e.* the first division is transverse, the second longitudinal.

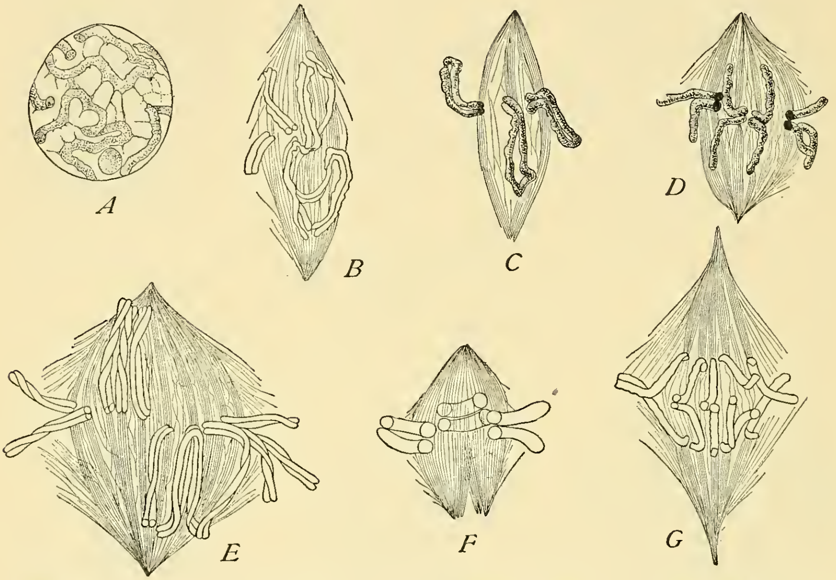

Fig. 134. — The second maturation-division in flowering plants. [*B.* Strasburger and Mottier; the others from Mottier.]

A. Nucleus of secondary spermatocyte (*Podophyllum*). *B.* Prophase of second division (*Lilium*, male) with longitudinally divided chromatin-threads. *E.* Corresponding stage in the female. *F.* Metaphase of second division (*Podophyllnm*, male). *G.* Initial anaphase (*Lilium*, female). *C. D.* illustrate Mottier's earlier conclusions. *C.* Second division (*Lilium*, male), with chromosomes bent together so as to simulate a split. *D.* Slightly later stage (*Fritillaria*, male), showing stage supposed to result from breaking apart of the limbs of the U at point of flexure.

point of attachment, thus giving rise to <>-shaped, -<>--shaped, or ××-shaped figures, all of which in the end assume the <>-shape. This part of the process is in the main similar to that described by Strasburger and Mottier, and the daughter-V's diverge in the same way as these authors describe. The second division, however, differs radically from their account, since no splitting of the spireme-thread occurs. The chromosomes reappear in the V-, Y-, and X-forms, but are *undivided*, and only half as thick as in the first division. Passing to the equator of the spindle, the V- and Y-forms break apart at the apex, while the X-forms separate into the two branches of the X, the daughter-chromosomes having the form of rods slightly bent at the outer end to form a J-figure (Fig. 135, *R–T*). This division is, accordingly, a transverse or reducing one, which "corresponds completely to the reduction-division in the animal organism" ('98, 2, p. 33.) Atkinson ('99) reaches the same general result in *Trillium*, stating very positively that no longitudinal division occurs in the second mitosis, and believing that the daughter-V's of the first (heterotypical) mitosis retain their individuality throughout the ensuing pause, and break apart at the apex (reducing division) in the second mitosis. This observer finds further that in *Arisæma* the heterotypical rings of the first mitosis *condense into true tetrads*, by one longitudinal and one transverse division, but believes that in this case it is the *first* division that effects the reduction, as in the insects.

Such confusion in the results of the most competent observers of reduction in the flowering plants is itself a sufficient commentary on the very great difficulty and uncertainty of the subject; and it would be obviously premature to draw any positive conclusions until further research shall have cleared up the matter.[1]

---

[1] Strasburger's new book, entitled *Über Reduktionstheilung, Spindelbildung, Centrosomen und Cilienbildner im Pflanzenreich* (Jena, 1900), is received while this work is in press, too late for analysis in the text. In this treatise the author gives an exhaustive review of the entire subject, contributing also many new and important observations on *Lilium*, *Iris*, *Podophyllum*, *Tradescantia*, *Allium*, *Larix*, and several other forms. The general result of these renewed researches leads Strasburger to return, in the main, to his conclusions of 1895, with which agree, as stated above, the results of Guignard and Grégoire; and, in a careful critique of Belajeff's work, he shows how the results of this observer may be reconciled with his own. The essence of Strasburger's interpretation is as follows. In the prophases of the first division the chromosomes first undergo a longitudinal division, shorten to form double rods, and then again split lengthwise in a plane at right angles to the first. The following stages vary even in the same species (*Lilium*); and here lies the explanation of much of the divergence between the accounts of different observers. (1) In the typical case, the chromosomes are placed radially, with one end next the spindle; and, during the metaphase, they open apart along the first division-plane, from the spindle outwards, to form ⊢-shaped figures. These figures meanwhile open apart from the free end inwards along the second division-plane. Thus arise the characteristic <>-shaped figures, the daughter-V's having separated along the first (equatorial) division-plane, while the two limbs of each V have resulted, not through bending, but from a second (axial) split (Fig. 135, *E–H*). The

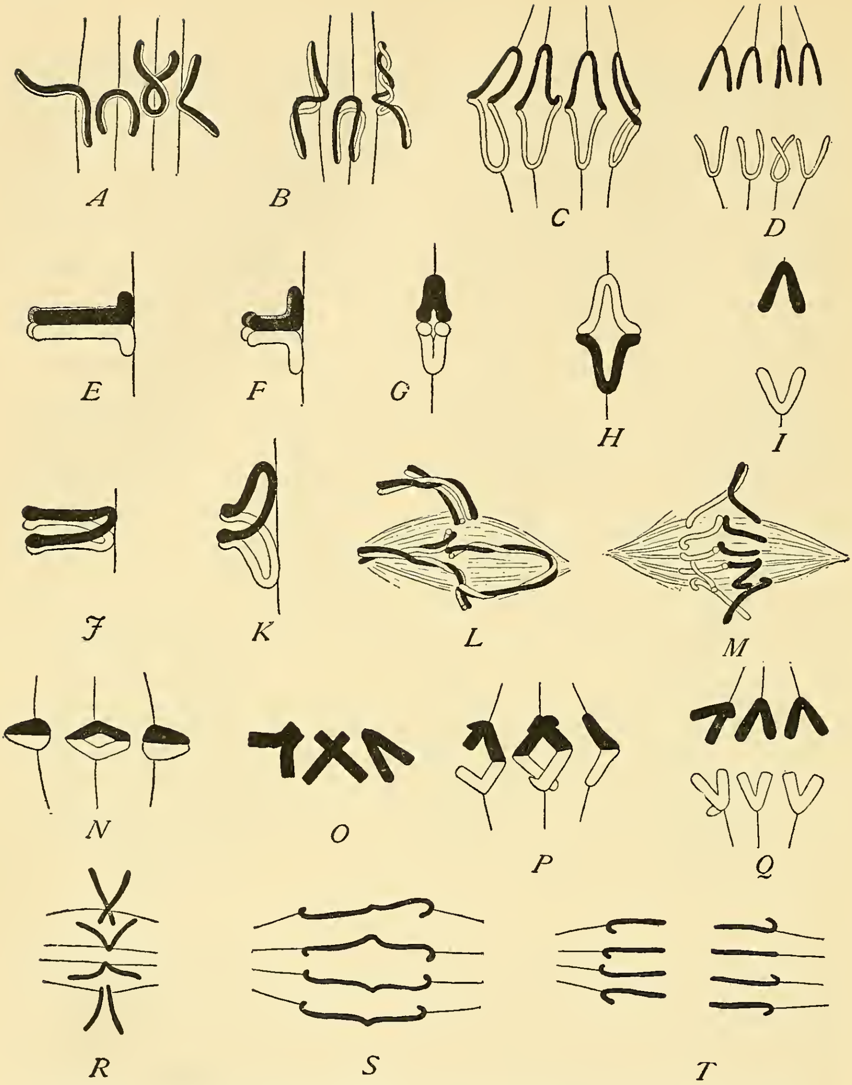

Fig. 135. — Diagrams illustrating different accounts of reduction in the flowering plants.

A–D. Vegetative mitoses (heterotypical form) in *Picea.* [BELAJEFF.]

E–I. Illustrate Strasburger's earlier account ('95) and the later one of Guignard, of the first maturation-division. *E.* Doubly split rod. *F.* Metaphase, in profile. *G.* The same *en face*, showing the heterotype ring. *H. I.* Opening out and breaking apart of the ring.

J–M. Later account of Strasburger and Mottier (*cf.* Figs. 133, 134). *J.* Longitudinally split, V-shaped chromosome of first division. *K.* Opening out of the ring. *L.* Prophase of second division, showing longitudinally split segmented spireme. *M.* Initial anaphase of second division.

N–Q. First division. [BELAJEFF.] *N.* Longitudinally split chromosomes, viewed in the equatorial plane. *O.* The same viewed in the axis of the spindle. *P.* Separation of the daughter-chromosomes. *Q.* Anaphase, all the chromosomes assuming the V-form.

R–T. Second division in *Iris.* [BELAJEFF.] *R.* Equatorial plate, limbs of X's and V's breaking apart (reducing division). *S.* Slightly later stage, with daughter-chromosomes still united at one end. *T.* Anaphase.

Résumé. In reduction without tetrad-formation the spireme segments into half the somatic number of chromosomes, which split lengthwise and open out to form rings for the first (heterotypical) mitosis. According to one set of observers, including Flemming, Meves, McGregor, Kingsbury, Moore, Klinckowström, Van der Stricht, Francotte, Griffin, Belajeff, Farmer, Dixon, Strasburger, Sargant, Mottier, Ishikawa, and Atkinson, the ring arises by a single longitudinal division. According to another group, including Carnoy, Le Brun, Guignard, and Grégoire, the ring arises through a double longitudinal division, one representing the axial and the other the equatorial plane of the <> -figure. The second group of observers regard both maturation-divisions as longitudinal. Among the first group, Flemming, Meves, McGregor, Kingsbury, Moore, Farmer, Dixon, Strasburger, Sargant, and Mottier likewise believe both divisions to be longitudinal, the daughter-V's or their products again splitting lengthwise for the second division; while Klinckowström, Van der Stricht, Francotte, Griffin, Belajeff, Ishikawa, and Atkinson believe one of them to be transverse, the daughter-V's breaking apart at the apex, and thus giving the reducing division of Weismann.[1]

D. Some Peculiarities of Reduction in the Insects

We may here briefly consider some interesting observations which show that in some cases the nuclear substance may be unequally distributed to the germ-nuclei. Henking ('90) discovered that in the second spermatocyte-division of *Pyrrochoris* one of the "chromosomes" passes undivided into one of the daughter-cells (spermatids) which receives twelve chromatin-elements while its sister receives but eleven. (The number of chromosomes in the spermatogonia, and of rings in the first spermatocyte-division is twenty-four). This anomalous process is confirmed with interesting additional details by Paulmier ('99) in *Anasa*, and obviously related phenomena are described by Montgomery ('99, 1) in *Pentatoma*, and by McClung ('99) in *Xiphidium*.

---

breaking apart of the V's at the apex, as described by Belajeff, is, therefore, not a transverse division, but merely the completion of the second longitudinal division. (2) In a second and exceptional type, the chromosomes are placed *tangentially* to the spindle, and the halves separate from the middle, again producing <> -shaped figures. These, however, are not of the same nature as those arising in the first case, since they are formed by a bending out of each daughter-chromosome at the middle to form the V, and not by the second longitudinal split. The effect of the latter is in this case to render each daughter-V in itself double, precisely as in the salamander. The difference between the two types results merely from the difference of position of the chromosome with respect to the spindle, and the final result is the same in both, *i.e.* two longitudinal divisions and no reducing one.

This highly important work brings very strong evidence against the occurrence of transverse or reducing divisions in the higher plants, and seems to explain satisfactorily most of the differences of interpretation given by other observers. It will be interesting to see whether a similar interpretation is possible in the case of mollusks, annelids, and arthropods, where the early stages, in many cases, so strikingly resemble those occurring in the plants.

[1] *Cf.* footnote on page 269.

In *Pentatoma* the number of chromosomes in the spermatocyte is fourteen. During the final anaphases of the last division, one of the fourteen daughter-chromosomes assumes a different staining-capacity from the others, and becomes a "chromatin-nucleolus" which fragments into several smaller bodies during the ensuing resting-stage. During each of the succeeding spermatocyte-divisions appear seven chromosomes and a single small chromatin-nucleolus, and both of these kinds of bodies are halved at each division, so that each spermatid receives seven chromosomes and a single chromatin-nucleolus.[1] In *Xiphidium* a body called by McClung the "accessory chromosome," and believed by him to correspond to the "chromatin-nucleolus" of *Pentatoma*, appears in the early prophases of the last spermatogonium-division while the remaining chromatin still forms a reticulum. In the equatorial plate this lies outside the ring of chromosomes, but divides like the latter. The same body appears in the ensuing resting-stage, and during both of the spermatocyte-divisions. In these it lies, as before, outside the chromosome-ring, and differs markedly from the other chromosomes, but divides like the latter, each of the halves passing into one of the spermatids, where it appears to form an important part of the sperm-nucleus.

Despite the peculiarities described above, the chromatin, as a whole, seems to be equally distributed in both *Pentatoma* and *Xiphidium*. In *Anasa*, however, Paulmier's studies ('98, '99), made in my laboratory, give a result agreeing with that of Henking, and suggest some very interesting further questions. The spermatogonia-nuclei contain two nucleolus-like bodies, and give rise to twenty-two chromosomes, of which two are smaller than the others (Fig. 126). In the first spermatocyte-division appear eleven tetrads. Ten of these arise from rings like those of *Gryllotalpa*, etc. The eleventh, which is much smaller than the others, seems to arise from a single nucleolus-like body of the spermatocyte-nucleus, and by a process differing considerably from the others. All of these bodies are halved to form dyads at the first division. In the second spermatocyte-division (Fig. 127) the larger dyads divide to form single chromosomes in the usual manner. *The small dyad, however, fails to divide, passing over bodily into one of the spermatids.* In this case, therefore, half of the spermatids receive ten single chromosomes, while the remainder receive in addition a small dyad.

A comparison of the foregoing results indicates that the small tetrad (dyad) corresponds to the extra chromosome observed by Henking in *Pyrrochoris*, and perhaps also to the "accessory chromosome" of *Xiphidium*. Whether it corresponds to the "chromatin-nucleolus" of *Pentatoma* is not yet clear. The most remarkable of these strange phenomena is the formation of the small tetrad, which seems to be a non-essential element, since it does not contribute to all the spermatozoa. Paulmier is inclined to ascribe to it a vestigial significance, regarding it as a "degenerating" chromosome which has lost its functional value, though still undergoing in some measure its original morphological transformation; in this connection it should be pointed out that the spermatocyte-nucleolus, from which it seems to be derived, is represented in the spermatogonia by *two* such nucleoli, just as the single small tetrad is represented by two small chromosomes in the spermatogonia-mitoses. The real meaning of the phenomenon is, however, wholly conjectural.

E. THE EARLY HISTORY OF THE GERM-NUCLEI

There are many peculiarities in the early history of the germ-nuclei, both in plants and animals, that have a special interest in connection with the reduction-problem; and some of these have raised some remarkable questions regarding the origin of reduction. A large number of observers are now agreed that during the growth-period preceding the maturation-division (p. 236), in both sexes, the nucleus of the mother-cell (spermatogonium, oögonium), both in plants and in animals, passes through some of the changes preparatory to reduction at a very early period. Thus, in the egg the primary chromatin-rods are often present in the very young ovarian eggs, and from their first appearance are already split longitudinally.[1] Häcker ('92, 2) made the interesting discovery that in some of the copepods (*Canthocamptus*, *Cyclops*) these double rods could be traced back continuously to a double spireme-thread, following immediately upon the division of the last generation of oögonia, and that *at no period is a true reticulum formed in the germinal vesicle* (Fig. 136). In the following year Rückert ('93, 2) made a precisely similar discovery in the case of selachians. After division of the last generation of oögonia the daughter-chromosomes do not give rise to a reticulum, but split lengthwise, and persist in this condition throughout the entire growth-period of the egg. Rückert therefore concluded that the germinal vesicle of the selachians is to be regarded as a "daughter-spireme of the oögonium (*Ur-ei*) grown to enormous dimensions, the chromosomes of which are doubled and arranged in

---

[1] On this latter point Montgomery's observations do not seem quite decisive.

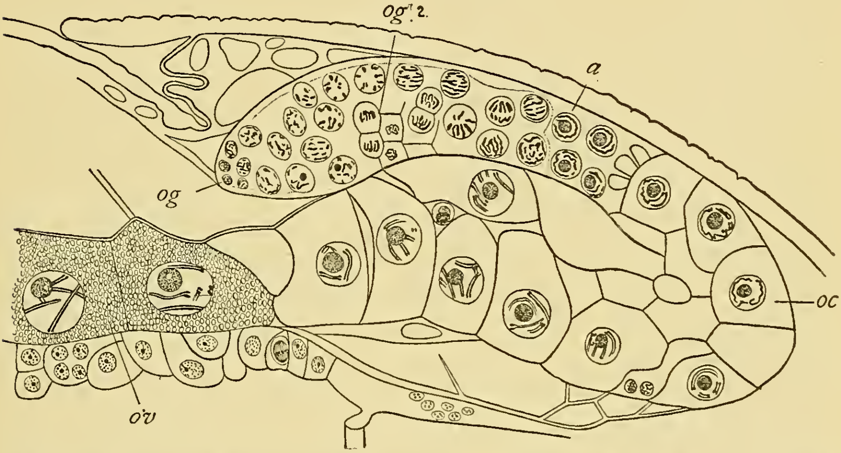

Fig. 136. — Longitudinal section through the ovary of the copepod *Canthocamptus*. [HÄCKER.] *og*. The youngest germ-cells or oögonia (dividing at *og*.^{2}); *a*. upper part of the growth-zone; *oc*. oöcyte, or growing ovarian egg; *ov*. fully formed egg, with double chromatin-rods.

---

[1] Häcker, Vom Rath, Rückert, in copepods; Rückert in selachians; Born and Fick in Amphibia; Holl in the chick; Rückert in the rabbit.

pairs."[1] In this case their number seems to be at first the somatic number (thirty-six), which is afterward halved by conjugation of the elements two and two (Rückert), as in *Lumbricus* (Calkins). It is, however, certain that in many cases (insects, copepods) the double rods first appear in the reduced number, and the observations of Vom Rath ('93) and Häcker ('95, 3) give some reason to believe that the reduced number may in some forms be present in the earlier progenitors of the germ-cells, the former author having found but half the normal number in some of the embryonic cells of the salamander, while Häcker ('95, 3) finds that in *Cyclops brevicornis* the reduced number of chromosomes (twelve) appears in the primordial germ-cells which are differentiated in the blastula-stage (Fig. 74). He adds the interesting discovery that in this form the *somatic* nuclei of the cleavage-stages show the same number, and hence concludes that all the chromosomes of these stages are bivalent. As development proceeds, the germ-cells retain this character, while the somatic cells acquire the usual number (twenty-four) — a process which, if the conception of bivalent chromosomes be valid, must consist in the division of each bivalent rod into its two elements. We have here a wholly new light on the historical origin of reduction; for the pseudo-reduction of the germ-nuclei seems to be in this case a persistence of the embryonic condition, and we may therefore hope for a future explanation of the process by which it has in other cases been deferred until the penultimate cell-generation, as is certainly the fact in *Ascaris*.[2]

This leads to the consideration of some very interesting recent discoveries regarding the relation of reduction to the alternation of generations in the higher plants. As already stated (p. 263), Strasburger, Guignard, and other observers have found that in the angiosperms the two maturation-divisions are in both sexes followed by one or more divisions in which the reduced number persists. The cells thus formed are generally recognized as belonging to the vestiges of the sexual generation (prothallium) of the higher cryptogams, the pollen-grains (or their analogues in the female) corresponding to the asexual spores of the archegoniate cryptogams. We should, therefore, expect to find reduction in the latter forms occurring in the two corresponding divisions, by which the "tetrad" of spores is formed (as was first pointed out by Hartog, '91). Botanists were thus led to the surmise, first expressed by Overton in 1892, that the reduced number would be found to occur in the prothallium-cells derived from those spores.

---

[1] '92, 2, p. 51.

[2] It may be recalled that in *Ascaris* Boveri proved that the primordial germ-cells have the full number of chromosomes, and Hertwig clearly showed that this number is retained up to the last division of the spermatogonia. Ishikawa ('97) finds that in *Allium* the reduced number (eight) appears in the mitosis of the "Urpollenzellen" preceding the pollen-mother-cells. This is, however, contradicted by Mottier ('97, 2).

This surmise quickly became a certainty. Overton himself discovered ('93) that the cells of the endosperm in the gymnosperm *Ceratozamia* divide with the reduced number, namely eight; and Dixon observed the same fact in *Pinus* at the same time. In the following year Strasburger brought the matter to a definite conclusion in the case of a fern (*Osmunda*), showing that *all the cells of the prothallium, from the original spore-mother-cell onwards to the formation of the germ-cells, have one-half the number of chromosomes found in the asexual generation*, namely twelve instead of twenty-four; in other words, the reduction takes place in the formation of the spore from which the sexual generation arises, many cell-generations before the germ-cells are formed, indeed before the formation of the body from which these cells arise. Similar facts were determined by Farmer in *Pallavicinia*, one of the Hepaticæ, where all of the nuclei of the asexual generation (sporogonium) show eight chromosomes during division, those of the sexual generation (thallus) four. It now seems highly probable that this will be found a general rule.

The striking point in these, as in Häcker's observations, is that the numerical reduction takes place so long before the fertilization for which it is the obvious preparation. Speculating on the meaning of this remarkable fact, Strasburger advances the hypothesis that the reduced number is *the ancestral number* inherited from the ancestral type. The normal, *i.e.* somatic, number arose through conjugation by which the chromosomes of two germ-cells were brought together. Strasburger does not hesitate to apply the same conception to animals, and suggests that the four cells arising by the division of the oögonium (egg plus three polar bodies) represent the remains of a separate generation, now a mere remnant included in the body in somewhat the same manner that the rudimentary prothallium of angiosperms is included in the embryo-sac. This may seem a highly improbable conclusion, but it must not be forgotten that so able a zoölogist as Whitman expressed a nearly related thought, as long ago as 1878: "I interpret the formation of polar globules as *a relic of the primitive mode of asexual reproduction*."[1] Strasburger's view is exactly the reverse of this in identifying the polar bodies as the remains of a sexual generation; and as Häcker has pointed out ('98, p. 102), it is difficult to reconcile with the fact that true reduction appears to occur already in the unicellular organisms (p. 277). The hypothesis is nevertheless highly suggestive and one which suggests a quite new point of view for the study not only of maturation but also of the whole problem of sexuality.

We may now return to the consideration of some details. In a considerable number of forms, though not in all, the early prophase is

---

[1] '78, p. 262.

characterized, especially in the male, by a more or less complete concentration of the chromatin-substance at one side of the nucleus. This stage, to which Moore has given the name *synapsis* (Fig. 120, *A*), sometimes occurs when the spireme thread is already split (*Ascaris, Lilium*), sometimes before the division is visible (insects). In either case *the chromatin-segments emerge from the synapsis stage longitudinally divided and in the reduced number*, a fact which gives ground for the conclusion that the synapsis is in some way concerned with the rearrangement of the chromatin-substance involved in the numerical reduction. During the synapsis the nucleolus remains quite distinct from the chromatin, and in many cases it afterward persists beside the tetrads, in the formation of which it takes no part, to be cast out into the cytoplasm (Fig. 124) or to degenerate *in situ* during the first maturation-division.

A suggestive phenomena, described by several observers,[1] is the casting out of a large part of the nuclear reticulum of the germinal vesicle at the time the polar bodies are formed (Figs. 97, 128). In these cases (*Asterias, Polychœrus, Thalassema, Nereis*) only a small fraction of the chromatin-substance is preserved to form the chromosomes, the remainder degenerating in the cytoplasm.[2]

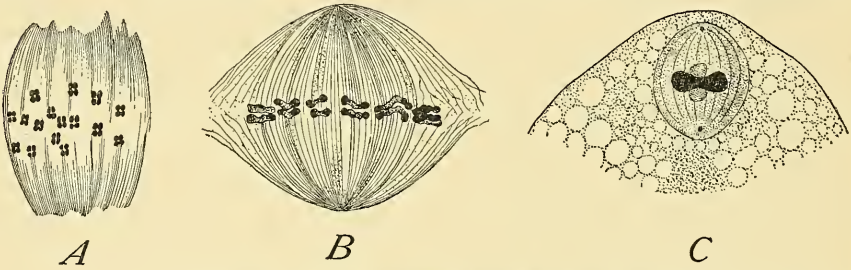

Fig. 137. — Types of maturation-spindles in the female.

A. First polar spindle with tetrads, in *Heterocope*. [HÄCKER]. *B.* Second polar spindle in *Triton*. [CARNOY and LEBRUN.] *C.* First polar spindle of *Ascaris*. [FÜRST.]

As a final point we must briefly consider the varying accounts of the achromatic maturation-figures in the female already briefly referred to at page 85. In many forms (*e.g.* in turbellarians, nemertines, annelids, mollusks, echinoderms) the polar amphiasters are of quite typical form, with large asters and distinct centrosomes nearly similar to those of the cleavage-figures. In others, however (nematodes, arthropods, tunicates, vertebrates), the polar spindles differ markedly from those of the cleavage-figures, being described by many authors as *entirely devoid of asters* and even in some cases of centrosomes (Fig. 137).

---

[1] *Cf.* Mathews (Wilson and Mathews, '95), Gardiner ('98), Griffin ('99).

[2] *Cf.* the enormous reduction of the chromatin-substance in the elasmobranch egg, p. 338.

There can be no doubt that these polar spindles differ from the usual type, and that they approach those recently described in the mitosis of the higher plants, but it is doubtful whether the apparent absence of asters and centrosomes is normal. In *Ascaris*, the first polar spindle arising by a direct transformation of the germinal vesicle (Fig. 117) has a barrel-shape, with no trace of asters. At the poles of the spindle, however, are one or two deeply staining granules (Fig. 137), which have been identified as centrosomes by Häcker ('94) and Erlanger ('97, 4), but by Fürst ('98) are regarded as central granules, the whole spindle being conceived as an enlarged centrosome.[1] For the reasons stated at page 314, I believe the former to be the correct interpretation.[2] Spindles without centrosomes have been described in the eggs of tunicates (Julin, Hill, Crampton), in *Amphioxus* (Sobotta), in some species of copepods (Häcker), and in some vertebrates (*Diemyctylus*, Jordan; mouse, Sobotta). In *Amphioxus* (Sobotta) and *Triton* (Carnoy and LeBrun) complete asters are not formed, but fibrillæ apparently corresponding to astral rays and converging to the spindle-poles are found outside the limits of the spindle (Fig. 137). In the guinea-pig, according to Montgomery ('98), centrosomes and asters are present in the first polar spindle, but absent in the second. The evidence is on the whole rather strong that the achromatic figure in these cases approaches in form that seen in the higher plants; but it is an open question whether the appearances described may not be a result of imperfect fixation.

F. Reduction in Unicellular Forms

Although the one-celled and other lower forms have not yet been sufficiently investigated, we have already good ground for the conclusion that a process analogous to the reduction of higher types regularly recurs in them. In the conjugation of Infusoria, as already described (p. 223), the original nucleus divides several times before union, and only one of the resulting nuclei becomes the conjugating germ-nucleus, while the others perish, like the polar bodies. The numerical correspondence between the rejected nuclei or "corpuscules de rebut" has already been pointed out (p. 227). Hertwig could not count the chromosomes with absolute certainty, yet he states ('89) that in *Paramæcium caudatum*, during the final division, the number of spindle-fibres and of the corresponding chromatic elements is but 4–6, while in the

---

[1] *Cf.* p. 312.

[2] Sala ('94) and Fürst have shown that occasionally the polar spindles of *Ascaris* are provided with large typical asters, and thus resemble those of annelids or mollusks. Sala believed this to be an effect of lowered temperature, but Fürst's observations are unfavourable to this conclusion.

earlier divisions the number is approximately double this (8–9). This observation makes it nearly certain that a numerical reduction of chromosomes occurs in the Protozoa in a manner similar to that of the higher forms; but the reduction here appears to be deferred until the final division. In the gregarines Wolters ('91) has observed the formation of an actual polar body as a small cell segmented off from each of the two conjugating animals soon after their union; but the number of chromosomes was not determined. Schaudinn ('96, 2) has observed a like process in *Actinophrys*, each of the gametes segmenting off a single polar body, after which the germ-nuclei fuse (Fig. 138). It is possible, as R. Hertwig ('98) points out, that in both these forms a second polar body may have been overlooked, owing perhaps to its rapid disintegration. In *Actinosphærium*, according to R. Hertwig ('98), the nucleus of each gamete divides twice in rapid succession to form two polar bodies (nuclei), which degenerate, after

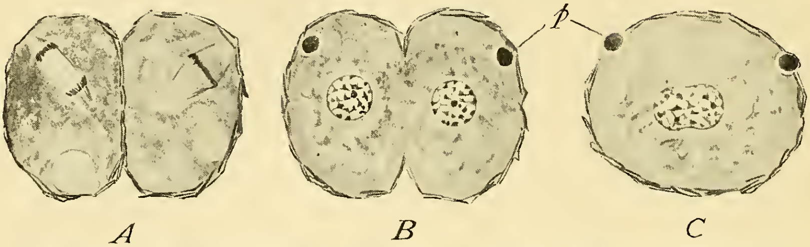

Fig. 138. — Conjugation and formation of the polar bodies in *Actinophrys*. [SCHAUDINN.]

A. Union of the gametes; first polar spindle. *B*. Fusion of the cell-bodies; a single polar body near the periphery of each. *C*. Fusion of the nuclei.

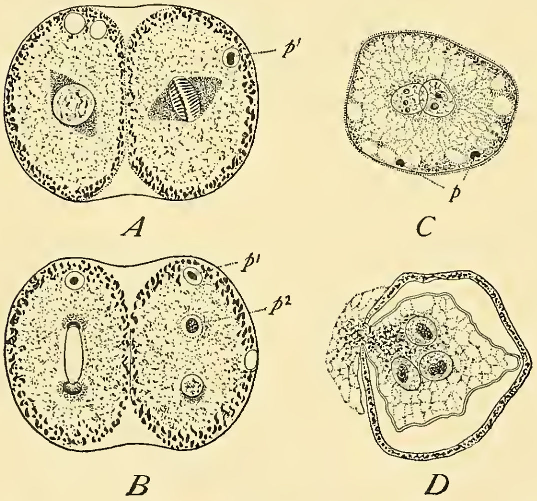

Fig. 139. — Formation of polar bodies and conjugation in *Actinosphærium*. [R. HERTWIG.]

A. Two gametes ("secondary cysts"), resulting from the division of a "primary cyst"; second maturation-spindle in each; first polar body shown in the right gamete, at *p*. *B*. Both polar bodies (p^1, p^2) formed in the right gamete, the second one forming in the left gamete. *C*. Subsequent fusion of the gametes; nuclei uniting, two polar bodies (probably the second, the first having been absorbed) at *p*. *D*. The young *Actinosphærium* escaping from the cyst-wall; the cleavage-nucleus has divided.

which the germ-nuclei unite (Fig. 139). Whether a reduction in the number of chromosomes occurs in these cases was not determined.[1]

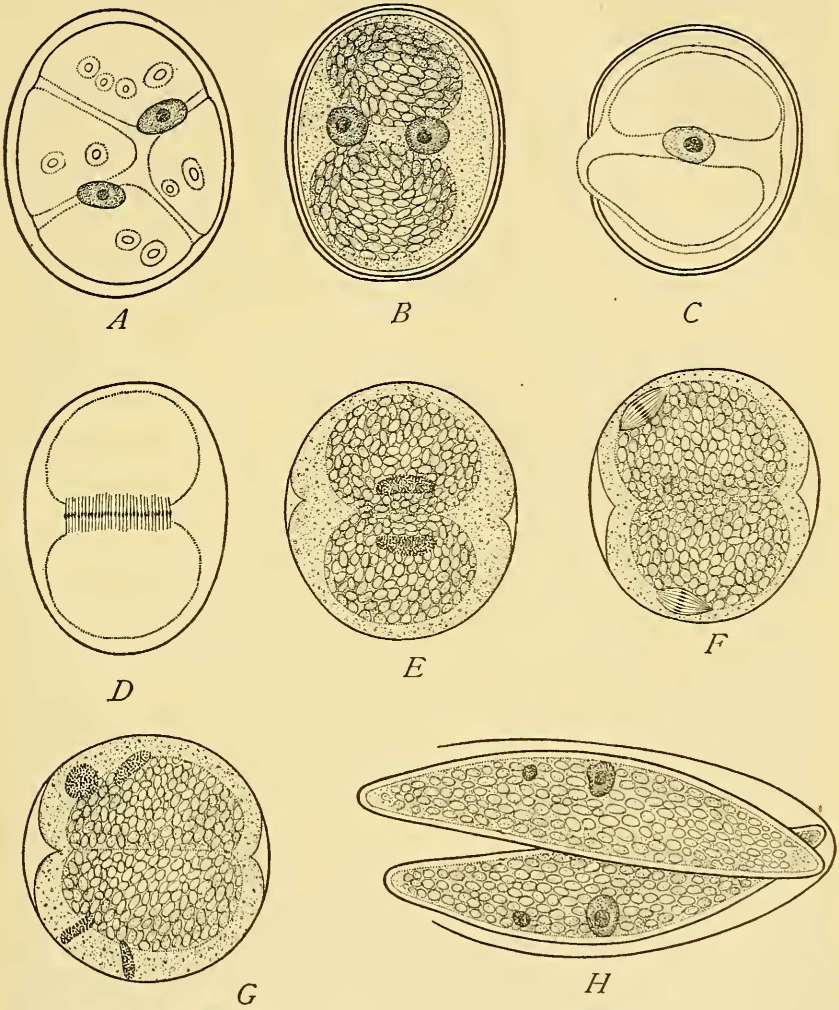

Fig. 140. — Conjugation of *Closterium*. [KLEBAHN.]

A. Soon after union, four chromatophores. *B.* Chromatophores reduced to two, nuclei distinct. *C.* Fusion of the nuclei. *D.* First cleavage of the zygote. *E.* Resulting 2-cell stage. *F.* Second cleavage. *G.* Resulting stage, each cell bi-nucleate. *H.* Separation of the cells; one of the nuclei in each enlarging to form the permanent nucleus, the other (probably representing a polar body) degenerating.

---

[1] *Actinosphærium* forms one of the most extreme known cases of in-breeding; for the gametes are *sister-cells* which immediately reunite after forming the polar bodies. The general facts are as follows: The mother animal, containing very numerous nuclei, becomes encysted, and a very large number of the nuclei degenerate. The body then segments into

Adelea (one of the Coccidiæ) is a very interesting case, for according to Siedlecki ('99) polar bodies or their analogues are formed in both sexes. The gametes are here of very unequal size. Upon their union the smaller male cell divides twice to form apparently equivalent spermatozoids, of which, however, only one enters the ovum, while three degenerate as polar bodies. These two divisions are of different type; the first resembles true mitosis, while the second is of simpler character and is believed by Siedlecki to effect a reduction in the number of chromosomes. In the meantime the nucleus of the macrogamete moves to the surface and there expels a portion of its chromatin, after which union of the nuclei takes place. Interesting facts have been observed in unicellular plants which indicate that the reduction may here occur either before (diatoms) or after (desmids) fusion of the conjugating nuclei. In the former (*Rhopalodina*) Klebahn ('96) finds that each nucleus divides twice, as in many Infusoria, giving rise to two large and two small nuclei. Each of the conjugates then divides, each daughter-cell receiving one large and one small nucleus. The four resulting individuals then conjugate, two and two, the large nuclei fusing while the small (polar bodies) degenerate. The comparison of this case with that of the Infusoria is highly interesting. In the desmids on the other hand (*Closterium* and *Cosmarium*, Fig. 140), according to Klebahn ('92), the nuclei first unite to form a cleavage-nucleus, after which the zygote divides into two. Each of the new nuclei now divides, one of the products persisting as the permanent nucleus, while the other degenerates and disappears. Chmielewski asserts that a similar process occurs in *Spirogyra*. Although the numerical relations of the chromosomes have not been determined in these cases, it appears probable that the elimination of a nucleus in each cell is a process of reduction occurring after fertilization.

G. MATURATION OF PARTHENOGENETIC EGGS

The maturation of eggs that develop without fertilization is a subject of special interest, partly because of its bearing on the general theory of fertilization, partly because it is here, as I believe, that one of the strongest supports is found for the hypothesis of the individuality of chromosomes. In an early article by Minot ('77) on the

---

a number (five to twelve) of "primary cysts," each containing one of the remaining nuclei. Each primary cyst divides by mitosis to form two gametes ("secondary cysts"), which, after forming the polar bodies, reunite, their nuclei fusing to form a single one. The resulting cell soon creeps out of the cyst-wall and assumes the active life, its nucleus meanwhile multiplying to produce the multinuclear condition characteristic of the adult animal. What is here the physiological motive for the formation of the polar bodies, and how shall it be explained under the Weismann hypothesis?

theoretical meaning of maturation, the suggestion is made that parthenogenesis may be due to failure on the part of the egg to form the polar bodies, the egg-nucleus thus remaining hermaphrodite, and hence capable of development without fertilization. This suggestion forms the germ of all later theories of parthenogenesis. Balfour ('80) suggested that the function of forming polar cells has been acquired by the ovum for the express purpose of preventing parthenogenesis, and a nearly similar view was afterward maintained by Van Beneden.[1] These authors assumed accordingly that in parthenogenetic eggs no polar bodies are formed. Weismann ('86) soon discovered, however, that the parthenogenetic eggs of *Polyphemus* (one of the Daphnidæ) produce a *single* polar body. This observation was quickly followed by the still more significant discovery by Blochmann ('88) that *in Aphis the parthenogenetic eggs produce a single polar body, while the fertilized eggs produce two.* Weismann was able to determine the same fact in ostracodes and Rotifera, and was thus led to the view[2] which later researches have entirely confirmed, that it is the *second* polar body that is of special significance in parthenogenesis. Blochmann observed that in insects the polar bodies were not actually thrown out of the egg, but remained embedded in its substance near the periphery. At the same time Boveri ('87, 1) discovered that in *Ascaris* the second polar body might in exceptional cases remain in the egg and there give rise to a resting-nucleus indistinguishable from the egg-nucleus or sperm-nucleus. He was thus led to the interesting suggestion that parthenogenesis might be due to the retention of the second polar body in the egg and its union with the egg-nucleus. "The second polar body would thus, in a certain sense, assume the *rôle* of the spermatozoön, and it might not without reason be said: "*Parthenogenesis is the result of fertilization by the second polar body.*"[3]

This conclusion received a brilliant confirmation through the observations of Brauer ('93) on the parthenogenetic egg of *Artemia*, though it appeared that Boveri arrived at only a part of the truth. Blochmann ('88–'89) had found that in the parthenogenetic eggs of the honey-bee *two* polar bodies are formed, and Platner discovered the same fact in the butterfly *Liparis* ('89) — a fact which seemed to contradict Boveri's hypothesis. Brauer's beautiful researches resolved the contradiction by showing that there are *two types* of *parthenogenesis* which may occur in the same animal. In the one case Boveri's conception is exactly realized, while the other is easily brought into relation with it.

(*a*) In both modes typical tetrads are formed in the germ-nucleus to the number of eighty-four. In the first and more frequent case

---

[1] '83, p. 622.

[2] Essay VI., p. 359.

[3] *l.c.*, p. 73.

(Fig. 141) but one polar body is formed, which removes eighty-four dyads, leaving eighty-four in the egg. There may be an abortive attempt to form a second polar spindle, but no division results, and the eighty-four dyads give rise to a reticular cleavage-nucleus. From this arise eighty-four thread-like chromosomes, and *the same number appears in later cleavage-stages.*

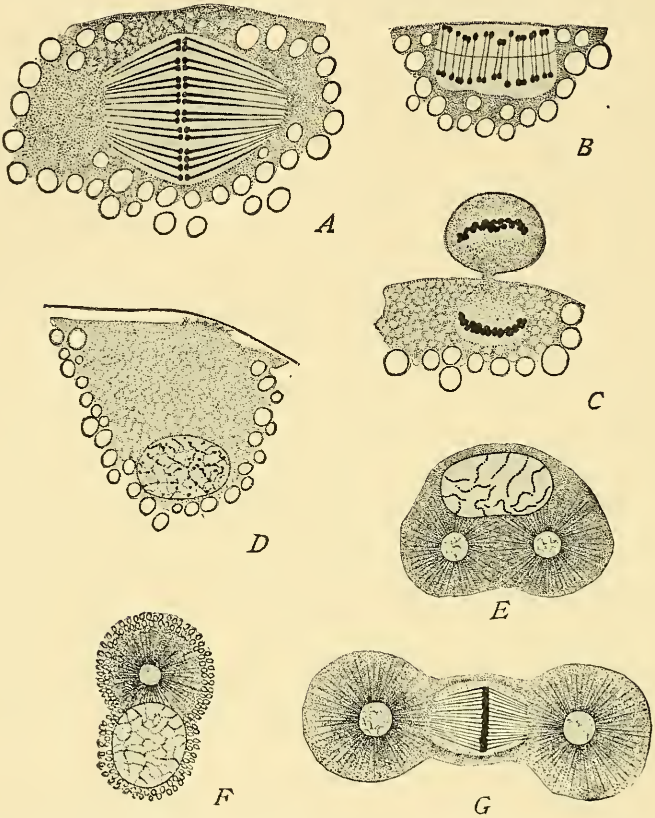

Fig. 141. — First type of maturation in the parthenogenetic egg of *Artemia*. [BRAUER.]

A. The first polar spindle; the equatorial plate contains 84 tetrads. *B. C.* Formation of the first polar body; 84 dyads remain in the egg, and these give rise to the egg-nucleus, shown in *D. F.* Appearance of the egg-centrosome and aster. *E. G.* Division of the aster and formation of the cleavage-figure; the equatorial plate consists of 84 apparently single but in reality bivalent chromosomes.

(*b*) It is the second and rarer mode that realizes Boveri's conception (Fig. 142). Both polar bodies are formed, the first removing eighty-four dyads and leaving the same number in the egg. In the formation of the second, the eighty-four dyads are halved to form two daughter-groups, each containing eighty-four single chromosomes. *Both these groups remain in the egg, and each gives rise to a single reticular nucleus, as described by Boveri in Ascaris. These two nuclei place themselves side by side in the cleavage-figure, and give rise each to eighty-four chromosomes, precisely like two germ-nuclei in ordinary fertilization.* The one hundred and sixty-eight chromosomes split lengthwise, and are distributed in the usual manner, *and reappear in the same number in later stages:* In other words, the second polar body here plays the part of a sperm-nucleus precisely as maintained by Boveri.

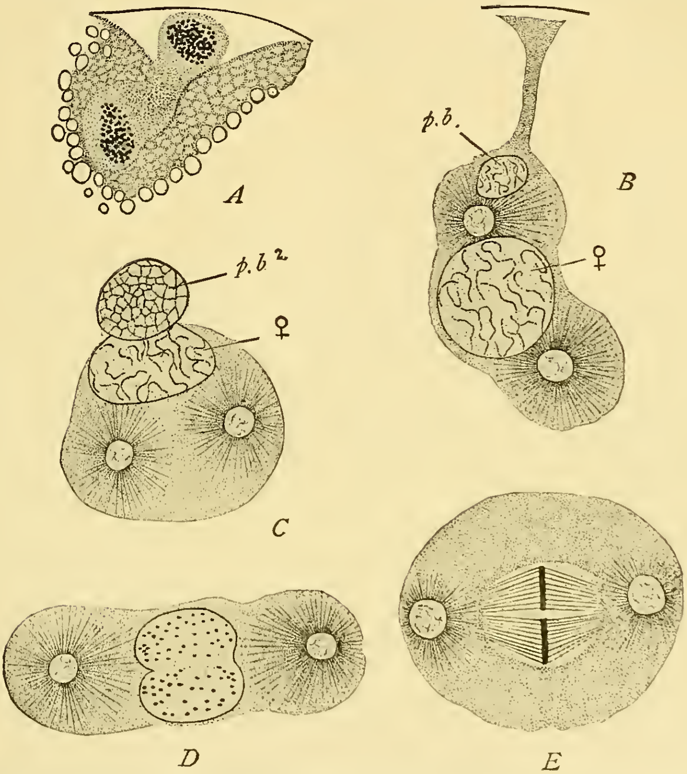

Fig. 142. — Second type of maturation in the parthenogenetic egg of *Artemia*. [BRAUER.]

A. Formation of second polar body. *B.* Return of the second polar nucleus (*p. b.*²) into the egg; development of the egg-amphiaster. *C.* Union of the egg-nucleus (♀) with the second polar nucleus (*p. b.*²). *D.* Cleavage-nucleus and amphiaster. *E.* First cleavage-figure with equatorial plate containing 168 chromosomes in two groups of 84 each.

In all individuals arising from eggs of the first type, therefore, the somatic number of chromosomes is eighty-four; in all those arising from eggs of the second type, it is one hundred and sixty-eight. This difference is clearly due to the fact that in the latter case the chromosomes are single or univalent, while in the former they are bivalent (actually arising from dyads or double chromosomes). The remarkable feature, on which too much emphasis cannot be laid, is that the numerical difference should persist despite the fact that the mass, and, as far as we can see, the quality, of the chromatin is the same in both cases. In this fact we must recognize a strong support, not only of Häcker's and Vom Rath's conception of bivalent chromosomes, but also of the more general hypothesis of the individuality of chromosomes (Chapter VI.).

1. *Accessory Cells of the Testis*

It is necessary to touch here on the nature of the so-called "Sertoli-cells," or supporting cells of the testis in mammals, partly because of the theoretical significance attached to them by Minot, partly because of their relations to the question of amitosis in the testis. In the seminiferous tubules of the mammalian testis, the parent-cells of the spermatozoa develop from the periphery inwards toward the lumen, where the spermatozoa are finally formed and set free. At the periphery is a layer of cells next the basement-membrane, having flat, oval nuclei. Within this, the cells are arranged in columns alternating more or less regularly with long, clear cells, containing large nuclei. The latter are the *Sertoli-cells*, or supporting cells; they extend nearly through from the basement-membrane to the lumen, and to their inner ends the young spermatozoa are attached by their heads, and there complete their growth. The spermatozoa are developed from cells which lie in columns between the Sertoli-cells, and which undoubtedly represent spermatogonia, spermatocytes, and spermatids, though their precise relationship is, to some extent, in doubt. The innermost of these cells, next the lumen, are spermatids, which, after their formation, are found attached to the Sertoli-cells, and are there converted into spermatozoa without further division. The deeper cells from which they arise are spermatocytes, and the spermatogonia lie deeper still, being probably represented by the large, rounded cells.

Two entirely different interpretations of the Sertoli-cells were advanced as long ago as 1871, and both views still have their adherents. Von Ebner ('71) at first regarded the Sertoli-cell as the parent-cell of the group of spermatozoa attached to it, and the same view was afterward especially advocated by Biondi ('85) and by Minot ('92), the latter of whom regarded the nucleus of the Sertoli-cell as the physiological analogue of the polar bodies, *i.e.* as containing the female nuclear substance ('92, p. 77). According to the opposing view, first suggested by Merkel ('71), the Sertoli-cell is not the parent-cell, but a nurse-cell, the spermatozoa developing from the columns of rounded cells, and becoming *secondarily* attached to the Sertoli-cell, which serves merely as a support and a means of conveying nourishment to the growing spermatozoa. This view was advocated by Brown ('85), and especially by Benda ('87). In the following year ('88), von Ebner himself abandoned his early hypothesis and strongly advocated Benda's views, adding the very significant result that *four spermatids arise from each spermatocyte*, precisely as was afterward shown to be the case in *Ascaris*, etc. The very careful and thorough work of Benda and von Ebner, confirmed by that of Lenhossék ('98, 2), leaves no doubt that mammalian spermatogenesis conforms, in its main outlines, with that of *Ascaris*, the salamander, and other forms, and that Biondi's account is untenable. Minot's theoretical interpretation of the Sertoli-cell, as the physiological equivalent of the polar bodies, therefore collapses.

2. *Amitosis in the Early Sex-cells*

Whether the progenitors of the germ-cells ever divide amitotically is a question of high theoretical interest. Numerous observers have described amitotic division in testis-cells, and a few also in those of the ovary. The recent observations of Meves ('91), Vom Rath ('93), and others leave no doubt whatever that such divisions occur in the testis of many animals. Vom Rath maintains, after an extended investigation, that all cells so dividing do not belong in the cycle of development of the germ-cells ('93, p. 164); that amitosis occurs only in the supporting or nutritive cells (Sertoli-cells, etc.), or in such as are destined to degenerate, like the "residual bodies" of Van Beneden. Meves has, however, produced strong evidence ('94) that in the salamander the spermatogonia may, in the autumn, divide by amitosis, and in the ensuing spring may again resume the process of mitotic division, and give rise to functional spermatozoa. On the strength of these observations Flemming ('93) himself now admits the possibility that amitosis may form part of a normal cycle of development.[1]

H. Summary and Conclusion

The one fact of maturation that stands out with perfect clearness and certainty amid all the controversies surrounding it is a *reduction of the number of chromosomes in the ultimate germ-cells to one-half the number characteristic of the somatic cells.* It is equally clear that this reduction is a preparation of the germ-cells for their subsequent union, and a means by which the number of chromosomes is held constant in the species. With a few exceptions the first indication of the numerical reduction appears through the segmentation of the spireme-thread, or the resolution of the nuclear reticulum, into a number of masses *one-half that of the somatic chromosomes.* In nearly all higher animals this process first takes place two cell-generations before the formation of the definitive germ-cells, and the process of reduction is completed by two rapidly succeeding "maturation-divisions," giving rise to four cells, all of which become functional in the male, while in the female only one becomes the egg, while the other three — the polar bodies or their analogues — are cast aside. During these two divisions each of the original chromatin-masses gives rise to four chromosomes, of which each of the four daughter-cells receives one; hence, each of the latter receives one-half the somatic number of chromosomes. In the higher plants, however, the two maturation-divisions are followed by a number of others, in which the reduced number of chromosomes persists, a process most strikingly shown in the pteridophytes, where a separate sexual generation (prothallium) thus arises, all the cells of which show the reduced number.

Two general types of maturation may be distinguished according to the manner in which the primary chromatin-masses divide. In one, typically represented by *Ascaris* and the arthropods, each of these masses divides into four to form a tetrad, thus preparing at once for two rapidly succeeding divisions, which are not separated by a reconstruction of the daughter-nuclei during an intervening resting period. In the other, examples of which are given by the flowering plants and the spermatogenesis of the Amphibia, no true tetrads are formed, the primary chromatin-masses dividing separately for each of the maturation-divisions, which are separated by a period in which the nuclei regress toward the resting state, though often not completely returning to the reticular condition. These two types differ, however, only in degree, and with few exceptions they agree in the fact that during the prophases of the first division the chromatin-bodies assume the form of rings, the mitosis thus being of the heterotypical form, and each ring having the prospective value of four chromosomes.

---

[1] For more recent literature on this subject see Meves, *Zelltheilung*, in Merkel and Bonnet's *Ergebnisse*, VIII., 1898.

Thus far the phenomena present no difficulty, and they give us a clear view of the process by which the numerical reduction of the *chromosomes* is effected. The confusion of the subject arises, on the one hand, from its complication with theories regarding the individuality of the chromosomes and the functions of chromatin in inheritance, on the other through conflicting results of observation on the mode of tetrad-formation and the character of the maturation-divisions. Regarding the latter question nearly all observers are now agreed that one of these divisions, usually the first, is a longitudinal or equation-division, essentially like that occurring in ordinary mitosis. The main question turns upon the other division, which has been shown in some cases to be transverse and not longitudinal, and thus separates what were originally different regions of the spireme-thread or nuclear substance. The evidence in favour of such a division seems at present well-nigh demonstrative in the case of insects and copepods, and hardly less convincing in the turbellarians, annelids, and mollusks. On the other hand, both divisions are regarded as longitudinal by most of those who have investigated the phenomena in *Ascaris* and in the vertebrates, and by some of the most competent investigators of the flowering plants.

The evidence as it stands is so evenly balanced that the subject is hardly yet ripe for discussion. The principle for which Weismann contended in his theory of reducing division has received strong support in fact; yet should it be finally established that numerical reduction may be effected either with or without transverse division, as now seems probable, not only will that theory have to be abandoned or wholly remodelled, but we shall have to seek a new basis for the interpretation of mitosis in general. Weismann's theory is no doubt of a highly artificial character; but this should not close our eyes to the great interest of the problem that it attempted to solve.

The existing contradiction of results has led to the opinion, expressed by a number of recent writers, that the difference between longitudinal or transverse division is of minor importance, and that the entire question of reduction is a barren one. This opinion fails to reckon with the facts on which rests the hypothesis of the individuality of chromosomes (Chap. VI.); but these facts cannot be left out of account. We must find a common basis of interpretation for them and for the phenomena of reduction; yet how shall we reconcile them with reduction by longitudinal division only? I cannot, therefore, share the opinion that we are dealing with a barren problem. The peculiarities of the maturation-mitoses are obviously correlated in some way with the numerical reduction, and the fact that they differ in so many ways from the characters of ordinary mitosis gives ground to hope that their exhaustive study will throw further light not only on the reduction-problem itself but also on mitosis in general and on still wider problems relating to the individuality of the chromosomes and the morphological organization of the nucleus. It is indeed very probable that Weismann's theory is but a rude attempt to attack the problem, and one that may prove to have been futile. The problem itself cannot be ignored, nor can it be dissociated from the series of kindred problems of which it forms a part.

LITERATURE. V[1]

Van Beneden, E. — Recherches sur la maturation de l'œuf, la fécondation et la division cellulaire: *Arch. Biol.*, IV. 1883.

Boveri, Th. — Zellenstudien, I., III. *Jena*, 1887–90. See also "Befruchtung" (List IV.).

Brauer, A. — Zur Kenntniss der Spermatogenese von *Ascaris megalocephala: Arch. mik. Anat.*, XLII. 1893.

Id. — Zur Kenntniss der Reifung der parthenogenetisch sich entwickelnden Eies von *Artemia Salina: Arch. mik. Anat.*, XLIII. 1894.

Guignard, L. — Le développement du pollen et la réduction chromatique dans le *Naias: Arch. Anat. Mic.*, II. 1899. (Full literature on reduction in plants.)

Griffin, B. B. — See Literature, IV.

Häcker, V. — Die Vorstadien der Eireifung (General Review): *Arch. mik. Anat.*, XLV. 2. 1895.

Id. — Über weitere Übereinstimmungen zwischen den Fertpflanzungsvorgängen der Thiere und Pflanzen: *Biol. Centralb.*, XVII. 1897.

Id. — Über vorbereitende Theilungsvorgänge bei Thieren und Pflanzen: *Verh. deutsch. Zool. Ges.*, VIII. 1898.

Id. — Die Reifungserscheinungen: *Merkel und Bonnet's Ergebnisse*. VIII. 1898.

Hertwig, O. — Vergleich der Ei- und Samenbildung bei Nematoden. Eine Grundlage für celluläre Streitfragen: *Arch. mik. Anat.*, XXXVI. 1890.

Mark, E. L. — (See List IV.)

Peter, K. — Die Bedeutung der Nährzellen im Hoden: *Arch. mik. Anat.*, LIII. 1898.

---

[1] See also Literature, IV., p. 231.

Platner, G. — Über die Bedeutung der Richtungskörperchen: *Biol. Centralb.*, VIII. 1889.

Vom Rath, O. — Zur Kenntniss der Spermatogenese von *Gryllotalpa vulgaris: Arch. mik. Anat.*, XL. 1892.

Id. — Neue Beiträge zur Frage der Chromatinreduktion in der Samen- und Eireife: *Arch. mik. Anat.*, XLVI. 1895.

Rückert, J. — Die Chromatinreduktion der Chromosomenzahl im Entwicklungsgang der Organismen: *Ergebn. d. Anat. u. Entwick.*, III. 1893 (1894).

Strasburger, E. — Über periodische Reduktion der Chromosomenzahl im Entwicklungsgang der Organismen: *Biol. Centralb.*, XIV. 1894.

Id. — Reduktionstheilung. Spindelbildung, etc.: *Jena, Fischer*, 1900.

CHAPTER VI

SOME PROBLEMS OF CELL-ORGANIZATION

> "Wir müssen deshalb den lebenden Zellen, abgesehen von der Molecularstructur der organischen Verbindungen, welche sie enthält, noch eine andere und in anderer Weise complicirte Structur zuschreiben, und diese es ist, welche wir mit dem Namen *Organization* bezeichnen."
>
> BRÜCKE.[1]

> "Was diese Zelle eigentlich ist, darüber existieren sehr verschiedene Ansichten."
>
> HÄCKEL.[2]

THE remarkable history of the chromatic substance in the maturation of the germ-cells forces upon our attention the problem of the ultimate morphological organization of the nucleus, and this in its turn involves our whole conception of protoplasm and the cell. The grosser and more obvious organization is revealed to us by the microscope as a differentiation of its substance into nucleus, cytoplasm, and the like. But, as Strasburger has well said, it would indeed be a strange accident if the highest powers of our present microscopes had laid bare the ultimate organization of the cell. Brücke insisted more than thirty years ago that protoplasm must possess a far more complicated morphological organization than is revealed to us in the visible structure of the cell, repeating, though without accepting, an earlier suggestion of Henle's ('41) that the cell might be composed of more elementary vital units ranking between the molecule and the cell. Many biological thinkers since Brücke's time have in one form or other accepted this conception, which indeed lies at the root of nearly all recent attempts to analyze exhaustively the phenomena of cell-life. Without attempting to follow out the history of opinion in detail or to give any extended review of the various theories,[3] it may be pointed out that this conception was based both on theoretical *a priori* grounds and on the observed facts of cell-structure. On the former basis it was developed by Herbert Spencer[4] in his theory of "physiological units" by which he endeavoured to explain the phenomena of regeneration, development, and heredity; while Nägeli ('84) developed on the same general lines his theory of *micellæ* which has been so widely accepted by botanists. In the meantime Darwin[1] introduced a new element into the speculative edifice in his celebrated hypothesis of pangenesis, where for the first time appear the two assumptions of specific differences in the ultra-microscopic corpuscles ("gemmules") and the power of self-propagation by division. Darwin did not, however, definitely maintain that protoplasm was actually built of such bodies. The latter hypothesis was added by De Vries ('89), who remodelled the theory of pangenesis on this assumption, thus laying the basis for the theories of development which reached their climax in the writings of Hertwig and Weismann.

---

[1] *Elementarorganismen*, 1861, p. 386.

[2] *Anthropogenie*, 1891, p. 104.

[3] For an exhaustive review see Yves Delage, *La structure du protoplasma et les théories sur l'hérédité*. Paris, 1895.

[4] *Principles of Biology*, 1864.

The views of Spencer and Darwin were based on purely theoretical grounds derived from the general phenomena of growth and inheritance.[2] Those of Nägeli, De Vries, Wiesner, Altmann, and others were more directly based on the results of microscopical investigation. The view was first suggested by Henle ('41), and at a later period developed by Béchamp and Estor, by Maggi and especially by Altmann, that the protoplasmic granules might be actually organic units or bioblasts, capable of assimilation, growth, and division, and hence to be regarded as elementary units of structure standing between the cell and the ultimate molecules of living matter. By Altmann, especially, this view was pushed to an extreme limit, which lay far beyond anything justified by the known facts; and the theory of genetic continuity expressed by Redi in the aphorism "*omne vivum ex vivo*," reduced by Virchow to "*omnis cellula e cellula*," finally appears in the writings of Altmann as "*omne granulum e granulo*"![3]

Altmann's premature generalization rested upon a very insecure foundation and was received with just scepticism. Except in the case of plastids, the division of the cytoplasmic granules was and still remains a pure assumption, and furthermore many of Altmann's "granules" (zymogen-granules of gland-cells, etc.) are undoubtedly metaplasmic bodies.[4] Yet the beautiful discoveries of Schimper ('85) and others on the origin of plastids in plant-cells give evidence that these cells do in fact contain large numbers of bodies, other than the nuclei, that possess the power of growth and division. The division of the chlorophyll-bodies, observed long ago by Mohl, was shown by Schmitz and Schimper to be their usual if not their only mode of origin; and Schimper was able to trace them back to minute colourless plastids, scarcely larger than "microsomes," that are present in large numbers in the protoplasm of the embryonic cells and of the egg, and give rise not only to chlorophyll-bodies but also to the amyloplasts or starch-formers and the chromoplasts or pigment-bodies. While it still remains doubtful whether the plastids arise solely by division or also by new formation (as now seems to be the case with the centrosome), the foregoing observations on the plastids give a substantial basis for the hypothesis that protoplasm may be built of minute dividing bodies which form its ultimate structural basis. It was these facts, taken in connection with the phenomena of particulate inheritance and variation (Galton), that led De Vries and his followers to the fundamental assumption of · "pangens," "plasomes," "biophores," and the like as final protoplasmic units;[1] but these were conceived not as the visible granules, plastids, etc., but as much smaller bodies, lying far beyond the limits of present microscopical vision, through the growth or aggregation of which the visible structures arise. This assumption has been harshly criticised; yet when we recall that in one form or another it has been accepted by such men as Spencer, Darwin, Beale, Häckel, Michael Foster, Nägeli, De Vries, Wiesner, Roux, Weismann, Oscar Hertwig, Verworn, and Whitman, and on evidence drawn from sources so diverse, we must admit that despite its highly speculative character it is not to be lightly rejected. In the present chapter we may inquire how far the known facts of cell-structure speak for or against this hypothesis, incidentally considering a number of detailed questions of cell-morphology which have not hitherto found a place.

---

[1] *Variation of Animals and Plants*, 1868.

[2] *Cf.* Introduction, p. 12.

[3] *Die Elementarorganismen*, Leipsic, 1894, p. 155.

[4] *Cf.* Lazarus, '98.

A. THE NATURE OF CELL-ORGANS

The cell is, in Brücke's words, an *elementary organism*, which may by itself perform all the characteristic operations of life, as is the case with the unicellular organisms, and in a sense also with the germ-cells. Even when the cell is but a constituent unit of a higher grade of organization, as in multicellular forms, it is no less truly an organism, and in a measure leads an independent life, even though its functions be restricted and subordinated to the common life. It is true that the earlier conception of the multicellular body as a colony of one-celled forms cannot be accepted without certain reservations.[2] Nevertheless, all the facts at our command indicate that the tissue-cell possesses the same morphological organization as the egg-cell, or the protozoan, and the same fundamental physiological properties as well. Like these the tissue-cell has its differentiated structural parts or organs, and we have now to inquire how these cell-organs are to be conceived.

---

[1] The following list includes only some of the various names that have been given to these hypothetical units by modern writers: *Physiological units* (Spencer); *gemmules* (Darwin); *pangens* (De Vries); *plasomes* (Wiesner); *micellæ* (Nägeli); *plastidules* (Häckel and Elssberg); *inotagmata* (Engelmann); *biophores* (Weismann); *bioblasts* (Beale); *somacules* (Foster); *idioblasts* (Hertwig); *idiosomes* (Whitman); *biogens* (Verworn); *microzymas* (Béchamp and Estor); *gemmæ* (Haacke). These names are not strictly synonymous, nor do all of the writers cited assume the power of division in the units.

[2] *Cf.* p. 58.

The visible organs of the cell fall under two categories, according as they are merely temporary structures, formed anew in each successive cell-generation out of the common structural basis, or permanent structures whose identity is never lost, since they are directly handed on by division from cell to cell.[1] To the former category belong, in general, such structures as cilia, pseudopodia, and the like; to the latter, the nucleus, perhaps also the centrosomes, and the plastids of plant-cells. A peculiar interest attaches to the permanent cell-organs. Closely interrelated as these organs are, they nevertheless have a remarkable degree of morphological independence. They assimilate food, grow, divide, and perform their own characteristic actions like coexistent but independent organisms, of a lower grade than the cell, living together in colonial or symbiotic association. So striking is this morphological and physiological autonomy in the case of the green plastids or chromatophores that neither botanists nor zoölogists are as yet able to distinguish with absolute certainty between those that form an integral part of the cell, as in the higher green plants, and those that are actually independent organisms living symbiotically within it, as is probably the case with the yellow cells of Radiolaria. Even so acute an investigator as Watasé ('93, 1) has seriously propounded the view that the nucleus itself — or rather the chromosome — should be regarded as a distinct organism living in symbiotic association with the cytoplasm, but having had, in an historical sense, a different origin. This rather fantastic view has not found much favour, and even were it true would teach us nothing of the origin of the power of division, which must for the present be taken as an elementary process forming one of the primary data of biology. Yet we may still inquire whether the power of division shown by such protoplasmic masses as plastids, chromosomes, centrosomes, nucleoli, and nuclei may not have its root in a like power residing in ultimate protoplasmic units of which they are made up. Could we accept such a view, we might much more easily meet some puzzling cytological difficulties. For under this assumption the difference between transient and permanent cell-organs would become only one of degree, depending on the degree of cohesion between their structural components; and we could thus conceive, for example, how such a body as a centrosome might form, persist by division for a number of generations, and finally disintegrate. In connection with this it may be pointed out that even such a typical permanent organ as the nucleus does not persist *as such* during the ordinary form of division; for it loses its boundary and many of its other structural characters, becoming resolved into a group of separate chromosomes. What persists is here not the structural unit, but the characteristic substance which forms its essential constituent, and a large part even of this substance may be lost in the process. The term "persistent organ" is therefore used in rather a figurative sense, and if too literally understood may easily mislead us.

---

[1] *Cf.* footnote, p. 30.

With the foregoing considerations in mind let us turn to the actual structural relation of the cell-organs.

B. Structural Basis of the Cell

In Chapter I. some of the reasons have been given for the conclusion that none of the obvious structural features of protoplasm (fibrillæ, alveoli, granules, and the like) can be regarded as necessary or universal; and we may now inquire whether there is any evidence that such structures may have such a common structural basis as De Vries's theory assumes. I shall here take as a point of departure my observations on the structure of protoplasm in echinoderm-eggs, already briefly reviewed at page 28. The beautiful alveolar structure of these eggs is entirely of secondary origin, and all the visible structural elements arise during the growth of the eggs by the deposit and subsequent enlargement of minute spherical bodies, all apparently liquid drops, in a homogeneous or finely granular basis which is itself a liquid. Some of these spheres enlarge to form the alveolar spheres, while the homogeneous basis or continuous substance remains as the interalveolar material. Others remain much smaller to constitute the "microsomes" scattered through the interalveolar walls; and these bodies, like the alveolar spheres, are perfectly visible in life, as well as in section; they are therefore not coagulation-products or artifacts. From these three elements arise all the other structures observed in these eggs, deutoplasm-spheres (*Ophiura*) and pigment-bodies (*Arbacia*) being formed by further enlargement and chemical alteration of the alveolar spheres, while astral rays and spindle-fibres are differentiated out of the inter-alveolar material and microsomes.[1] These various elements show a continuous gradation in size from the largest deutoplasm-spheres down to the smallest visible granules, the latter being the source of all the larger elements, and in their turn emerging into view from the "homogeneous" basis. Clearly, then, none of these bodies can be regarded as the ultimate structural units; for the latter, if they exist, must lie in a region at present inaccessible to the microscope. This fact, however, no more disproves their existence than it does that of molecules and atoms. It only shows the futility of such attempts as those of Altmann and his predecessors to identify "granules" or "microsomes" as final morphological units, and compels us to turn to indirect instead of direct evidence. It may, however, again be pointed out that it would be quite irrational to conclude that the smallest visible granules first come into existence when they first come within view of the microscope. The "homogeneous" substance must itself contain or consist of granules still smaller. The real question is not whether such ultra-microscopical bodies exist, but whether they are permanent *organized* bodies possessing besides the power of growth also the power of division. This question can be only indirectly approached; and we shall find it convenient to do so by beginning at the opposite end of the series, through a reconsideration of the phenomena of nuclear division.

---

[1] *Cf.* Wilson, '99.

C. MORPHOLOGICAL COMPOSITION OF THE NUCLEUS

1. *The Chromatin*

(*a*) *Hypothesis of the Individuality of the Chromosomes.* — It may now be taken as a well-established fact that the nucleus is never formed *de novo*, but always arises by the division of a preëxisting nucleus. In the typical mode of division by mitosis the chromatic substance is resolved into a group of chromosomes, always the same in form and number in a given species of cell, and having the power of assimilation, growth, and division, as if they were morphological individuals of a lower order than the nucleus. That they are such individuals or units has been maintained as a definite hypothesis, especially by Rabl and Boveri. As a result of careful study of mitosis in epithelial cells of the salamander, Rabl ('85) concluded that *the chromosomes do not lose their individuality at the close of division, but persist in the chromatic reticulum of the resting nucleus.* The reticulum arises through a transformation of the chromosomes, which give off anastomosing branches, and thus give rise to the appearance of a network. Their loss of identity is, however, only apparent. They come into view again at the ensuing division, at the beginning of which "the chromatic substance flows back, through predetermined paths, into the primary chromosome-bodies" (Kernfäden), which reappear in the ensuing spireme-stage in nearly or quite the same position they occupied before. Even in the resting nucleus, Rabl believed that he could discover traces of the chromosomes in the configuration of the network, and he described the nucleus as showing a distinct polarity having a "pole" corresponding with the point toward which the apices of the chromosomes converge (*i.e.* toward the centrosome), and an "antipole" (Gegenpol) at the opposite point (*i.e.* toward the equator of the spindle) (Fig. 22). Rabl's hypothesis was precisely formulated and ardently advocated by Boveri in 1887 and 1888, and again in 1891, on the ground of his own studies and those of Van Beneden on the early stages of *Ascaris*. The hypothesis was supported by extremely strong evidence, derived especially from a study of abnormal variations in the early development of *Ascaris*, the force of which has, I think, been underestimated by the critics of the hypothesis. Some of this evidence may here be briefly reviewed. In some cases, through a miscarriage of the mitotic mechanism, one or both of the chromosomes destined for the second polar body are accidentally left in the egg. These chromosomes give rise in the egg to a reticular nucleus, indistinguishable from the egg-nucleus. At a later period this nucleus gives rise to the same number of chromosomes as those that entered into its formation, *i.e.* either one or two. These are drawn into the equatorial plate along with those derived from the germ-nuclei, and mitosis proceeds as usual, the number of chromosomes being, however, abnormally increased from four to five or six (Fig. 143,

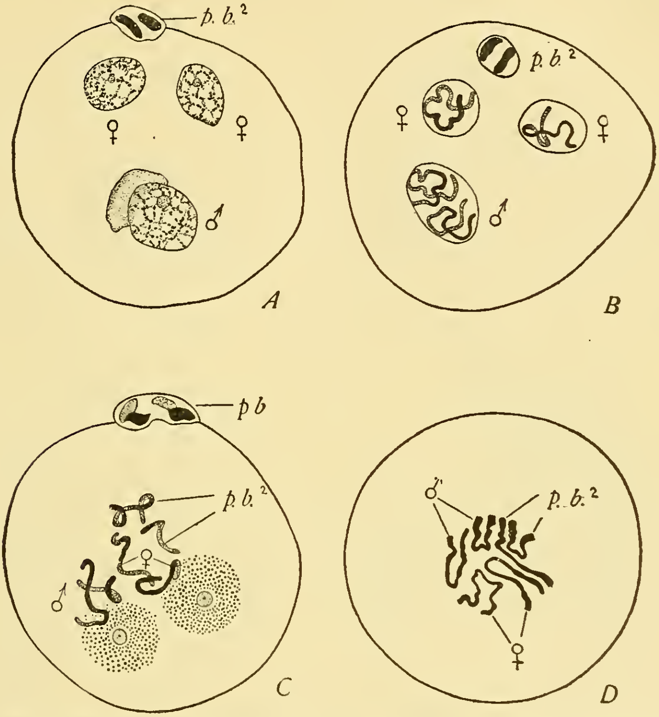

Fig. 143.—Evidence of the individuality of the chromosomes. Abnormalities in the fertilization of *Ascaris*. [Boveri.]

A. The two chromosomes of the egg-nucleus, accidentally separated, have given rise each to a reticular nucleus (♀, ♀); the sperm-nucleus below (♂). *B.* Later stage of the same, a single chromosome in each egg-nucleus, two in the sperm-nucleus. *C.* An egg in which the second polar body has been retained; $p.b.^2$ the two chromosomes arising from it; ♀ the egg-chromosomes; ♂ the sperm-chromosomes. *D.* Resulting equatorial plate with six chromosomes.

C, *D*). Again, the two chromosomes left in the egg after removal of the second polar body may accidentally become separated. In this case each chromosome gives rise to a reticular nucleus of half the usual size, and from each of these a *single* chromosome is afterward formed (Fig. 143, *A*, *B*). Finally, it sometimes happens that the two germ-nuclei completely fuse, while in the reticular state, as is normally the case in sea-urchins and some other animals (p. 188). From the cleavage-nucleus thus formed arise four chromosomes.

The same general result is given by the observations of Zur Strassen ('98) on the history of giant embryos in *Ascaris*. These embryos arise by the fusion, either before or after the fertilization, of previously separate eggs, and have been shown to be capable of development up to a late stage. Not only in the first but also in some, at least, of the later mitoses, such eggs show an increased number of chromosomes proportional to the number of nuclei that have united. Thus in monospermic double eggs (variety *bivalens*) the number is six instead of four; in dispermic double eggs the number is increased to eight (Fig. 144).

These remarkable observations show that *whatever be the number of chromosomes entering into the formation of a reticular nucleus, the same number afterward issues from it*—a result which demonstrates that the number of chromosomes is not due merely to the chemical composition of the chromatin-substance, but to a morphological organization of the nucleus. A beautiful confirmation of this conclusion was afterward made by Boveri ('93, '95, 1) and Morgan ('95, 4), in the case of echinoderms, by rearing larvæ from enucleated egg-fragments, fertilized by a single spermatozoön (p. 194). All the nuclei of such larvæ contain but half the typical number of chromosomes,—*i.e.* in *Echinus* nine instead of eighteen,—since all are descended from one germ-nucleus instead of two!

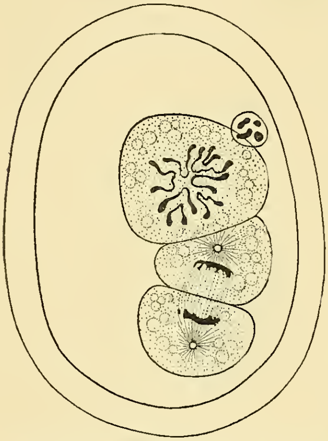

Fig. 144.—Giant-embryo of *Ascaris*, *var. bivalens*, arising from a double-fertilized double egg, showing eight chromosomes (*Zur Strassen*).

Equally striking is the remarkable fact, described at page 275, that all of the cells in the sexual generation (oöphore) of the higher cryptogams show half the number of chromosomes characteristic of the sporophyte, the explanation being that while reduction occurs at the time of spore-formation, the spores develop without fertilization, the reduced chromosome-number persisting until fertilization occurs long afterward. Attention may be again called to the surprising case of *Artemia*, described at page 281, which gives a strong argument in favour of the hypothesis.

In addition to the foregoing evidence, Van Beneden and Boveri were able to demonstrate in *Ascaris* that in the formation of the spireme the chromosomes reappear in the same position as those which entered into the formation of the reticulum, precisely as Rabl maintained. As the long chromosomes diverge, their free ends are always turned toward the middle plane (Fig. 31), and upon the reconstruction of the daughter-nuclei these ends give rise to corresponding lobes of the nucleus, as in Fig. 145, which persist throughout the resting state. At the succeeding division the chromosomes reappear exactly in the same position, *their ends lying in the nuclear lobes as before* (Fig. 145, *G*, *H*). On the strength of these facts Boveri concluded that the chromosomes must be regarded as "individuals" or "elementary organisms," that have an independent existence in the

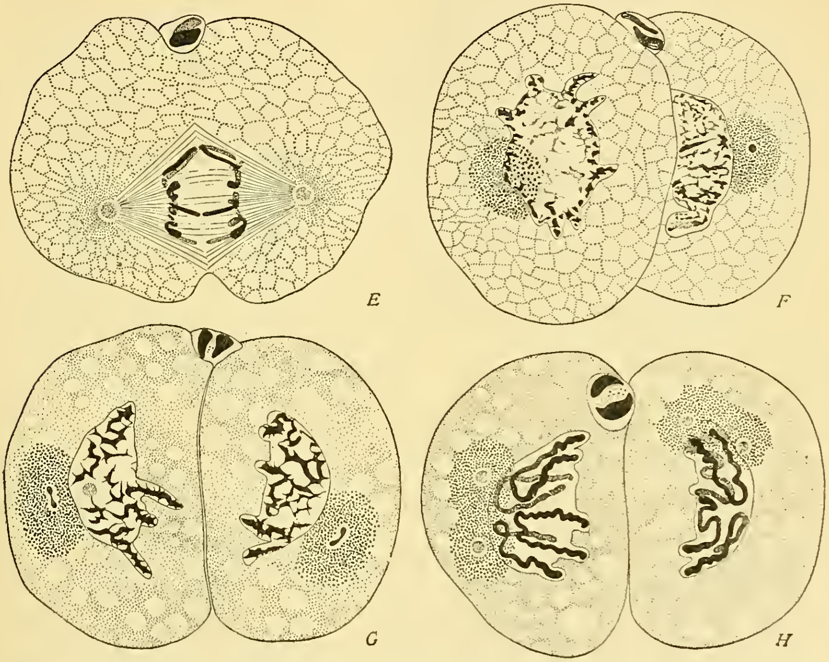

Fig. 145. — Evidence of the individuality of the chromosomes in the egg of *Ascaris*. [BOVERI.]

E. Anaphase of the first cleavage. *F.* Two-cell stage with lobed nuclei, the lobes formed by the ends of the chromosomes. *G.* Early prophase of the ensuing division; chromosomes re-forming, centrosomes dividing. *H.* Later prophase, the chromosomes lying with their ends in the same position as before; centrosomes divided.

cell. During the reconstruction of the nucleus they send forth pseudopodia which anastomose to form a network in which their identity is lost to view. As the cell prepares for division, however, the chromosomes contract, withdraw their processes, and return to their "resting state," in which fission takes place. Applying this conclusion to the fertilization of the egg, Boveri expressed his belief that "we may identify every chromatic element arising from a resting nucleus with a definite element that entered into the formation of that nucleus, from which the remarkable conclusion follows *that in all cells derived in the regular course of division from the fertilized egg, one-half of the chromosomes are of strictly paternal origin, the other half of maternal.*"[1]

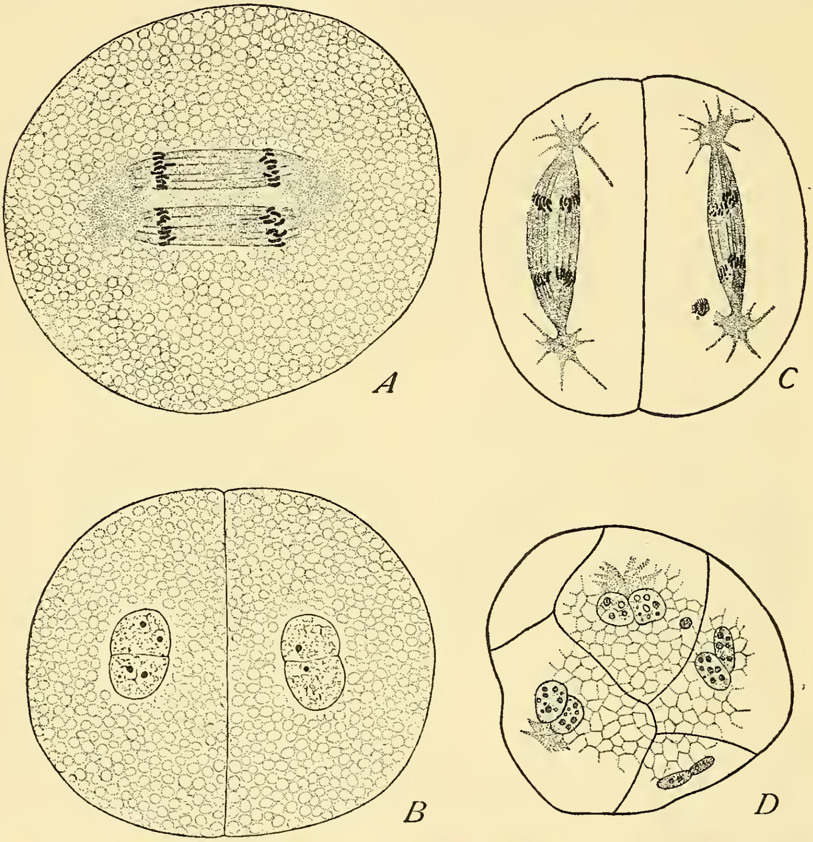

Fig. 146. — Independence of paternal and maternal chromatin in the segmenting eggs of *Cyclops*. [*A–C*, from RÜCKERT; *D*, from HÄCKER.]

A. First cleavage-figure in *C. strenuus;* complete independence of paternal and maternal chromosomes. *B*. Resulting two-cell stage with double nuclei. *C*. Second cleavage; chromosomes still in double groups. *D*. Blastomeres with double nuclei from the eight-cell stage of *C. brevicornis.*

---

[1] '91, p. 410.

Boveri's hypothesis has been criticised by many writers, especially by Hertwig, Guignard, and Brauer, and I myself have urged some objections to it. Recently, however, it has received a support so strong as to amount almost to a demonstration, through the remarkable observations of Rückert, Häcker, Herla, and Zoja on the independence of the paternal and maternal chromosomes. These observations, already referred to at page 208, may be more fully reviewed at this point. Häcker ('92, 2) first showed that in *Cyclops strenuus*, as in *Ascaris* and other forms, the germ-nuclei do not fuse, but give rise to two separate groups of chromosomes that lie side by side near the equator of the cleavage-spindle. In the two-cell stage (of *Cyclops tenuicornis*) each nucleus consists of two distinct though closely united halves, which Häcker believed to be the derivatives of the two respective germ-nuclei. The truth of this surmise was demonstrated three years later by Rückert ('95, 3) in a species of *Cyclops*, likewise identified as *C. strenuus* (Fig. 146). The number of chromosomes in each germ-nucleus is here twelve. Rückert was able to trace the paternal and maternal groups of daughter-chromosomes not only into the respective halves of the daughter-nuclei of the two-cell stage, but into *later cleavage-stages*. From the bilobed nuclei of the two-cell stage arise, in each cell, a double spireme and a double group of chromosomes, from which are formed bilobed or double nuclei in the four-cell stage. This process is repeated at the next cleavage, and the double character of the nuclei was in many cases distinctly recognizable at a late stage when the germ-layers were being formed.

Finally Victor Herla's ('93) and Zoja's ('95, 2) remarkable observations on *Ascaris* showed that in *Ascaris* not only the chromatin of the germ-nuclei, but also the paternal and maternal *chromosomes*, remain perfectly distinct as far as the twelve-cell stage — certainly a brilliant confirmation of Boveri's conclusion. Just how far the distinction is maintained is still uncertain, but Häcker's and Rückert's observations give some ground to believe that it may persist throughout the entire life of the embryo. Both these observers have shown that the chromosomes of the germinal vesicle appear in *two distinct groups*, and Rückert suggests that these may represent the paternal and maternal elements that have remained distinct throughout the entire cycle of development, even down to the formation of the egg!

Leaving aside all doubtful cases (such as the above suggestion of Rückert's), the well-determined facts form an irresistible proof of the general hypothesis; and it is one with which every general analysis of the cell has to reckon. I believe, however, that the hypothesis has received an unfortunate name; for, except in a few special cases,[1] almost no direct evidence exists to show that the chromosomes persist as "individuals" in the chromatin-reticulum of the resting cell. The facts indicate, on the contrary, that in the vast majority of cases the identity of the chromosomes is wholly lost in the resting nucleus, and the attempts to identify them through the polarity or other morphological features of the nuclear network have on the whole been futile. It is therefore an abuse of language to speak of a persistent "individuality" of chromosomes. But this verbal difficulty should not blind us to the extraordinary interest and significance of the facts. It is difficult to suppose that the tendency of the chromatin to resolve itself into a particular number of chromosomes is directly due to its chemical or molecular structure, or is analogous to crystallization; for in the chromatin of the same species, or even in that of the same egg, this tendency varies, not with chemical, but with purely morphological

---

[1] *Cf.* p. 273.

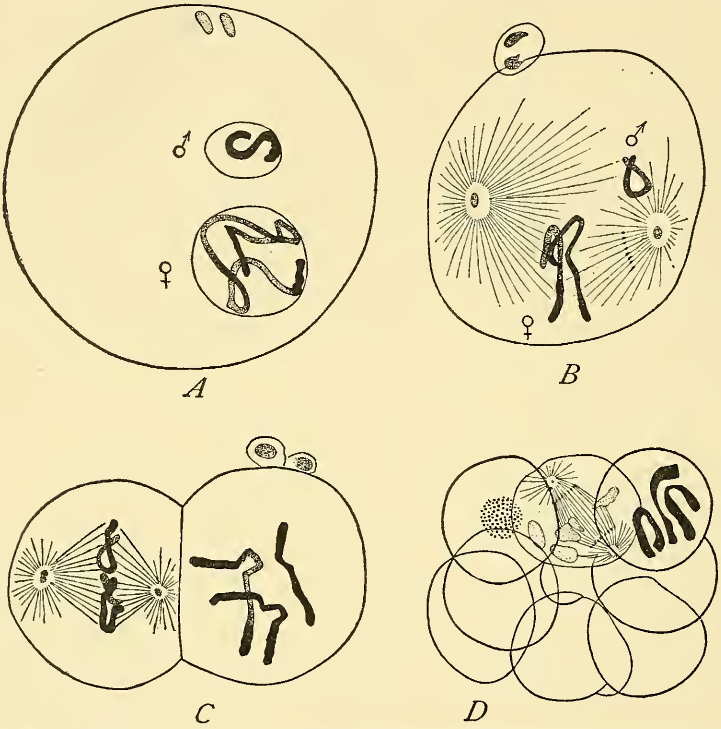

Fig. 147. — Hybrid fertilization of the egg of *Ascaris megalocephala*, var. *bivalens*, by the spermatozoön of var. *univalens*. [HERLA.]

A. The germ-nuclei shortly before union. *B*. The cleavage-figure forming; the sperm-nucleus has given rise to one chromosome (♂), the egg-nucleus to two (♀). *C*. Two-cell stage dividing, showing the three chromosomes in each cell. *D*. Twelve-cell stage, with the three distinct chromosomes still shown in the primordial germ-cell or stem-cell.

conditions, *i.e.* with the *number* of chromosomes that enter the nucleus. Neither can we assume that it is due merely to the total mass of the chromatin in each case; for this varies in different nuclei of the same species, or even in the nucleus of the same cell at different periods (as in the egg-cell), yet the same number of chromosomes is characteristic of all. Indeed, we seek in vain for an analogy to these phenomena and can only admit our entire inability to explain them. No phenomena in the history of the cell more clearly indicate the existence of a morphological organization which, though resting upon, is not to be confounded with, the chemical and molecular structure that underlies it; and this remains true even though we are wholly ignorant what that organization is.

(*b*) *Composition of the Chromosomes.* — We owe to Roux[1] the first clear formulation of the view that the chromosomes, or the chromatin-thread, consist of successive regions or elements that are qualitatively different (p. 244). This hypothesis, which has been accepted by Weismann, Strasburger, and a number of others, lends a peculiar interest to the morphological composition of the chromatic substance. The facts are now well established (1) that in a large number of cases the chromatin-thread consists of a series of granules (chromomeres) embedded in and held together by the linin-substance, (2) that the splitting of the chromosomes is caused by the division of these more elementary bodies, (3) that the chromatin-grains may divide at a time when the spireme is only just beginning to emerge from the reticulum of the resting nucleus. These facts point unmistakably to the conclusion that these granules are perhaps to be regarded as independent morphological elements of a lower grade than the chromosomes. That they are not artifacts or coagulation-products is proved by their uniform size and regular arrangement in the thread, especially when the thread is split. A decisive test of their morphological nature is, however, even more difficult than in the case of the chromosomes; for the chromatin-grains often become apparently fused together so that the chromatin-thread appears perfectly homogeneous, and whether they lose their individuality in this close union is undetermined. Observations on their number are still very scanty, but they point to some very interesting conclusions. In Boveri's figures of the egg-maturation of *Ascaris* each element of the tetrad consists of six chromatin-discs arranged in a linear series (Van Beneden's figures of the same object show at most five) which finally fuse to form an apparently homogeneous body. In the chromosomes of the germ-nuclei the number is at least double this (Van Beneden). Their number has been more carefully followed out in the spermatogenesis of the same animal (variety *bivalens*) by Brauer. At the time the chromatin-grains divide, in the reticulum of the spermatocyte-nucleus, they are very numerous. His figures of the spireme-thread show at first nearly forty granules in linear series (Fig. 120, *B*). Just before the breaking of the thread into two the number is reduced to ten or twelve (Fig. 120, *C*). Just after the division to form the two tetrads the number is four or five (Fig. 120, *D*), which finally fuse into a homogeneous body.[1]

---

[1] *Bedeutung der Kerntheilungsfiguren*, 1883, p. 15.

It is certain, therefore, that the number of chromomeres is not constant in a given species, but it is a significant fact that in *Ascaris* the final number, before fusion, appears to be nearly the same (four to six) both in the oögenesis and the spermatogenesis. The facts regarding bivalent and plurivalent chromosomes (p. 87) at once suggest themselves, and one cannot avoid the thought that the smallest chromatin-grains may successively group themselves in larger and larger combinations of which the final term is the chromosome. Whether these combinations are to be regarded as "individuals" is a question which can only lead to a barren play of words. The fact that cannot be escaped is that the history of the chromatin-substance reveals to us, not a homogeneous substance, but a definite morphological organization in which, as through an inverted telescope, we behold a series of more and more elementary groups, the last visible term of which is the smallest chromatin-granule, or nuclear microsome, beyond which our present optical appliances do not allow us to see. Are these the ultimate dividing units, as Brauer suggests (p. 113)? Here again we may well recall Strasburger's warning, and hesitate to identify the end of the series with the limits reached by our best lenses. Somewhere, however, the series must end in final chromatic units which cannot be further subdivided without the decomposition of chromatin into simpler chemical substances; and these units must be capable of assimilation, growth, and division without loss of their specific character. It is in these ultimate units that we must seek the "qualities," if they exist, postulated in Roux's hypothesis; but the existence of such qualitative differences is a physiological assumption that in no manner prejudices our conclusion regarding the ultimate *morphological* composition of the chromatin.

D. Chromatin, Linin, and Cytoplasm

What, now, is the relation of the chromatin-grains to the linin-network and the cytoplasm? Van Beneden long ago maintained[2] that the achromatic network, the nuclear membrane, and the cell-meshwork have essentially the same structure, all consisting of microsomes united by connective substance, and being only "parts of one and the same structure." But, more than this, he asserted that *the chromatic and achromatic microsomes might be transformed into one another, and were therefore of essentially the same morphological nature.* "They pass successively, in the course of the nuclear evolution, through a chromatic or an achromatic stage, according as they imbibe or give off the chromophilous substance."[1] Both these conclusions are borne out by recent researches. Heidenhain ('93, '94), confirmed by Reinke and Schloter, finds that the nuclear network contains granules of two kinds differing in their staining-capacity. The first are the basi-chromatin granules, which stain with the true nuclear dyes (basic tar-colours, etc.), and are identical with the "chromatin-granules" of other authors. The second are the oxychromatin-granules of the linin-network, which stain with the plasma-stains (acid colours, etc.), and are closely similar to those of the cytoreticulum. *These two forms graduate into one another, and are conjectured to be different phases of the same elements.* This conception is furthermore supported by many observations on the behaviour of the nuclear network as a whole. The chromatic substance is known to undergo very great changes in staining-capacity at different periods in the life of the nucleus (p. 338), and is known to vary greatly in bulk. In certain cases a very large amount of the original chromatic network is cast out of the nucleus at the time of the division, and is converted into cytoplasm. And, finally, in studying mitosis in sea-urchin eggs I found reason to conclude ('95, 2) that a considerable part of the linin-network, from which the spindle-fibres are formed, is actually derived from the chromatin.

---

[1] Eisen ('99) finds that the chromosomes of the spermatogonia of *Batrachoseps* always consist of six "chromomeres," each of which consists of three smaller granules or "chromioles." The latter persist as the chromatin-granules of the resting nucleus; and it is through their successive aggregation that the chromomeres and chromosomes are formed.

[2] '83, pp. 580, 583.

From the time of the earlier writings of Frommann ('65, '67), Arnold ('67), Heitzmann ('73), and Klein ('78), down to the present, an increasing number of observers have held that the nuclear reticulum is to be conceived as a modification of the same structural basis as that which forms the cytoplasm. The latest researches indicate, indeed, that true chromatin (nuclein) is confined to the nucleus.[2] But the whole weight of the evidence now goes to show that the linin-network is of the same nature as the cell-meshwork, and that the achromatic nuclear membrane is formed as a condensation of the same substance. Many investigators, among whom may be named Frommann, Leydig, Klein, Van Beneden, Carnoy, and Reinke, have described the fibres of both the intra- and extra-nuclear network as terminating in the nuclear membrane; and the membrane itself is described by these and other observers as being itself reticular in structure, and by some (Van Beneden) as consisting of closely crowded microsomes arranged in a network. The clearest evidence is, however, afforded by the origin of the spindle-fibres in mitotic division; for it is now well established that these may be formed either inside or outside the nucleus, and at the close of mitosis the central portion of the spindle appears always to give rise to a portion of the cytoplasm lying between the daughter-nuclei. In such a case as that of the sea-urchin (see above) we have, therefore, evidence of a direct transformation of chromatin into linin-substance, of the latter into spindle-fibres, and, finally, of these into cytoplasm.

---

[1] *l.c.* p. 583.

[2] *Cf.* Hammarsten ('95).

When all these facts are placed in connection, we find it difficult to escape the conclusion that no definite line can be drawn between the cytoplasmic granules at one extreme and the chromatin-granules at the other. And inasmuch as the latter are certainly capable of growth and division, we cannot deny the possibility that the former may themselves have, or arise from elements having like powers. But while we may take this as a fair working hypothesis, we should clearly recognize that the base of well-determined fact on which it rests is approached by a circuitous route; that in case of most of the cytoplasmic granules there is not the slightest evidence that they multiply by division; and that even though some of them may have such powers, we cannot regard them as the ultimate structural units, for the latter must be bodies far more minute.

E. The Centrosome

From our present point of view the centrosome possesses a peculiar interest as a cell-organ which may be scarcely larger than a cytomicrosome, yet possesses specific physiological properties, assimilates, grows, divides, and may persist from cell to cell without loss of identity. Nearly all observers of the centrosome have found it lying in the cytoplasm, outside the nucleus; but apart from the Protozoa (p. 94) there is at least one well-established case in which it lies within the nucleus, namely, that of *Ascaris*, where Brauer made the interesting discovery that *in one variety* (*univalens*) *the centrosome lies inside the nucleus, in the other variety* (*bivalens*) *outside* — a fact which proves that its position is non-essential (*cf.* Figs. 120 and 148).

An intra-nuclear origin of the centrosome has also been asserted by Julin ('93) in the primary spermatocytes of *Styleopsis*, by Rückert ('94) in the eggs of *Cyclops*, Mathews ('95) in those of *Asterias*, Carnoy and Le Brun ('97, 2) in *Ascaris*, Van der Stricht ('98) in the eggs of *Thysanozoön*, by R. Hertwig ('98) in *Actinosphærium*, Calkins ('98, 1) in *Noctiluca*, and Schaudinn ('96, 3) in spore-producing buds of *Acanthocystis*, though in the last-named form the centrosome of the vegetative forms is extra-nuclear (p. 92).

As already stated,[1] it is still undetermined whether a true centrosome may ever arise *de novo*, but the evidence in favour of such a possibility has of late rapidly increased. Carnoy ('86) long since showed that the egg of *Ascaris*, during the formation of the polar bodies, sometimes showed numerous accessory asters scattered through the cytoplasm. Reinke ('94) described somewhat similar asters in peritoneal cells of the salamander, distinguishing among them three orders of magnitude, the largest containing distinct centrosomes or "primary centres," while the smaller contained "secondary" and "tertiary" centres, the last named being single microsomes at the nodes of the cytoreticulum. By successive aggregations of the tertiary and secondary centres arise true centrosomes as new formations. Watasé ('94–'95) also finds in the egg of *Macrobdella*, besides the normal aster containing an undoubted centrosome, numerous smaller asters graduating downwards to such "tertiary asters" as Reinke describes with a microsome at the centre of each, and on this basis concludes that the true centrosome differs from a microsome only in degree and may arise *de novo*. Mottier ('97, 2) finds in pollen-mother-cells numerous minute "cyto-asters" having no direct relation to the spindle-formation (Fig. 133). Again Juel

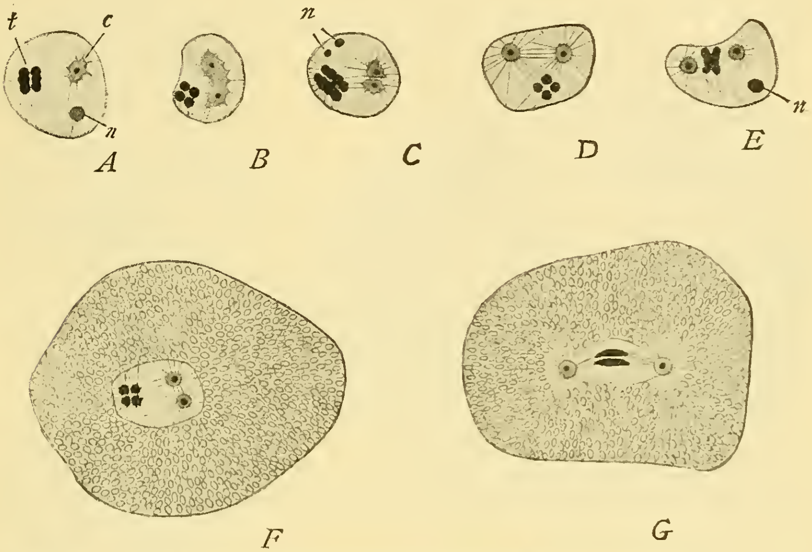

Fig. 148. — Mitosis with intra-nuclear centrosome, in the spermatocytes of *Ascaris megalocephala*, var. *univalens*. [Brauer.]

A. Nucleus containing a quadruple group or tetrad of chromosomes (*t*), nucleolus (*n*), and centrosome (*c*). *B. C.* Division of the centrosome. *D. E. F. G.* Formation of the mitotic figure, centrosomes escaping from the nucleus in *G*.

---

[1] *Cf.* pp. 52, 214.

('97) finds that an isolated chromosome, accidentally separated from the equatorial plate (pollen-mother-cells of *Hemerocallis*), may give rise to a small vesicular nucleus which may subsequently divide by mitosis, though it is quite out of relation to the spindle-poles of the preceding mitosis (Fig. 149). Strong evidence of the same character as the last is given by the facts in the heliozoön *Acanthocystis*, as shown by Schaudinn ('96, 3), the ordinary vegetative cells containing a persistent extra-nuclear centrosome, while in the bud-formation of the swarm-spores a centrosome is formed *de novo*, *without relation to that of the mother-cell*, inside the nucleus of the bud (Fig. 41).

The strongest case in favour of the independent origin of centrosomes is, however, given by the observations of Mead on *Chætopterus* ('98) and the remarkable experiments of R. Hertwig ('95, '96) and Morgan ('96, 1; '99, 1) on the eggs of echinoderms and other animals. When eggs of *Chætopterus* are taken from the body-cavity and placed in sea-water, a multitude of small asters appear in the cytoplasm, two of which are believed to persist as those of the polar spindle, while the others degenerate (Fig. 150). Mead is therefore convinced that the polar centrosomes arise in this case separately and *de novo*.[1] R. Hertwig showed that when unfertilized eggs of sea-urchins (*Strongylocentrotus*, *Echinus*) are kept for some time in sea-water or treated with dilute solutions of strychnine the nuclei undergo some of

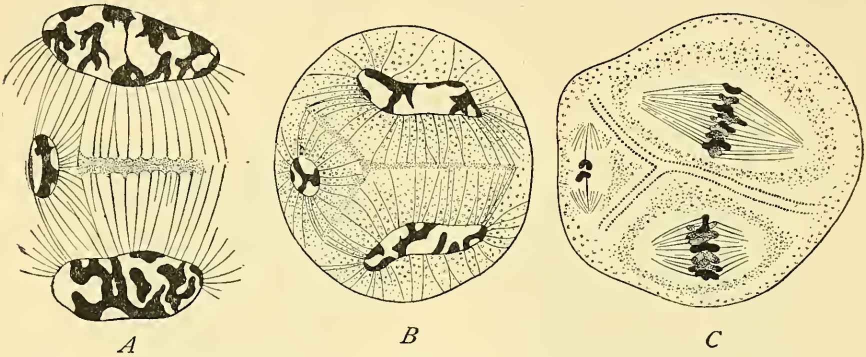

Fig. 149. — Abnormal mitosis in pollen-mother-cells of *Hemerocallis*, showing formation of small nucleus from one or two stray chromosomes and its subsequent division. [JUEL.]

---

[1] A number of other authors (*e.g.* Griffin, *Thalassema*, Coe, *Cerebratulus*) have likewise found the first polar asters widely separated at their first appearance. On the other hand, Mathews ('95), whose preparations I have seen, finds the polar centrosomes in *Asterias* close together, and Francotte ('97, '98) has demonstrated that in *Cycloporus* and *Prosthecerœus* they arise by the division of a single primary centrosome. The same is stated by Gardiner ('98) to be the case in *Polychœrus*. It should be noted, further, that Mead could find no undoubted centrosomes save in the "primary" or definitive polar asters.

the changes of mitosis, the chromatin-network giving rise to a group of chromosomes and a spindle, or more frequently a fan-shaped half-spindle, arising from the achromatic substance. In some cases not only a complete spindle appeared but also asters at the poles, though no centrosomes were observed (Fig. 151). Morgan's experiments along the same lines were mainly performed upon the sea-urchin *Arbacia*, but included also the eggs of *Asterias*, *Sipunculus*, and *Cerebratulus* (Figs. 150, 151). In these eggs numerous asters may arise in the cytoplasm, if they are allowed to lie some time in sea-water or treated by weak solutions of sodium or magnesium chloride. These asters often contain deeply staining, central granules indistinguishable from the centrosomes of the normal asters; and, what is of high interest, such of them as lie near the nucleus take part in the irregular nuclear division that ensues, forming centres toward which the chromosomes pass. These divisions continue for some time, the chromosomes being irregularly distributed through the egg, and giving rise to nuclei of various sizes apparently dependent upon the number of chromosomes each receives. After a variable number of such

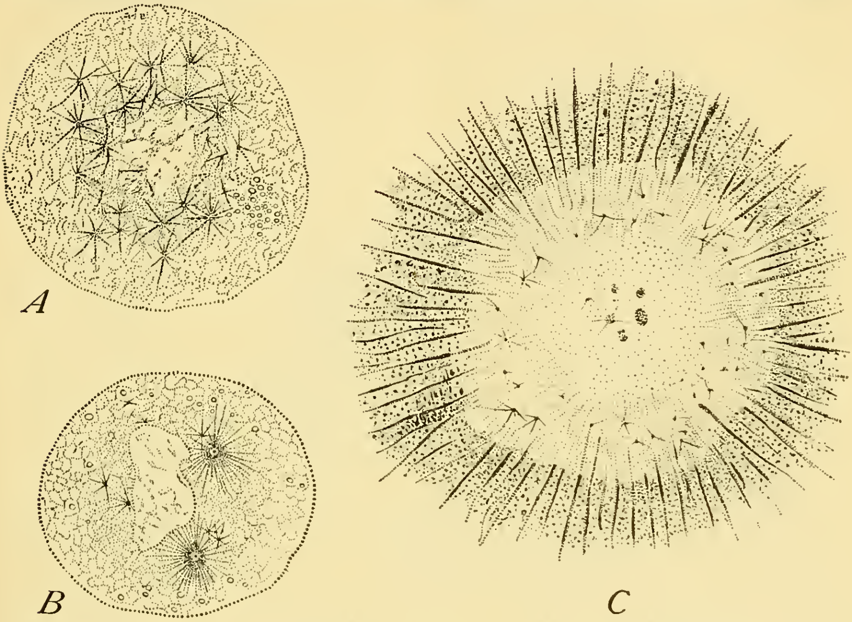

Fig. 150. — Formation *de novo* (?) of centrosomes. [*A*, *B*, MEAD; *C*, MORGAN.]

A. Unfertilized egg of *Chætopterus* with "secondary asters" developed a few minutes after the egg is placed in sea-water. *B*. Slightly later stage with two definitive polar asters and centrosomes. *C*. Large "sun" (transformed polar aster) containing numerous small "secondary asters" and centrosomes, from unfertilized egg of *Cerebratulus* after 22 hours in 1.5 % sodium chloride solution.

divisions the asters disappear, yet the irregular nuclear divisions continue, nuclear spindles with distinct centrosomes being formed at each division, but apparently without relation to the older asters, and they are believed by Morgan to arise *de novo* from the egg substance.[1] In the meantime irregular cleavage of the egg occurs, though no embryo is produced.[2] Loeb, however, in the remarkable experiments

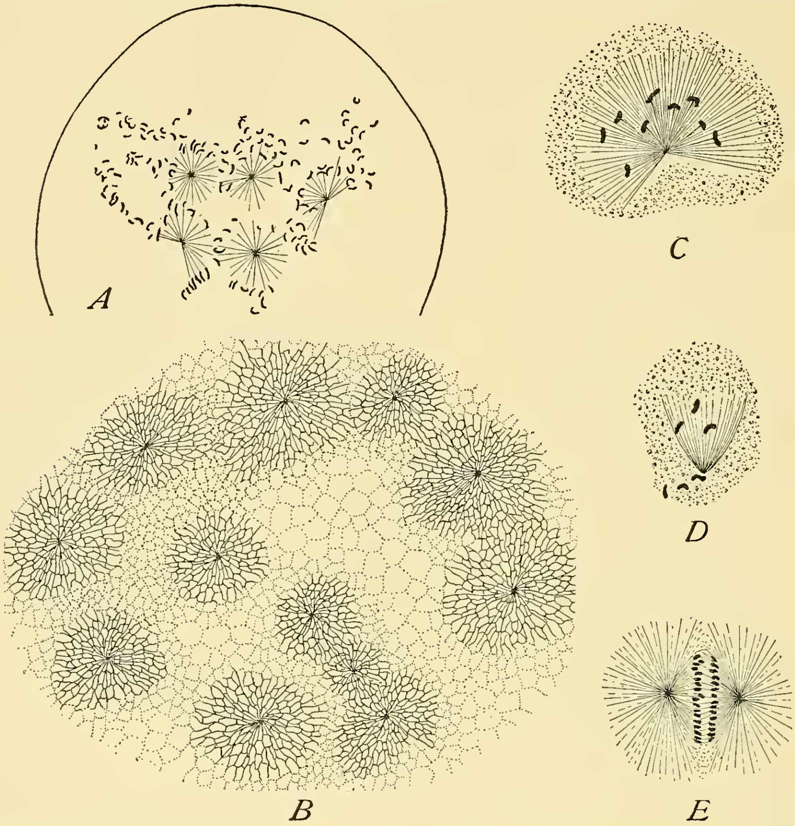

Fig. 151. — Formation of centrosomes and asters in unfertilized echinoderm-eggs. [*A, B,* MORGAN; *C–E,* R. HERTWIG.]

A. Arbacia, after 4½ hours in 1.5 % solution of sodium chloride, then 5 hours in sea-water; scattered chromosomes and asters. *B.* Asters formed after 6½ hours in NaCl. *C–E. Echinus* after treatment with 0.5 % strychnine-solution, showing various forms of astral formations (fan-shaped aster, half spindle, and complete mitotic figure).

---

[1] '99, p. 479.

[2] Morgan makes the important observation, which harmonizes with that of Boveri, reported at page 108, *that the divisions occur with respect to the number and position of the nuclei, not of the asters,* concluding that the former must therefore play an essential *rôle* as centres of division, and that the activity of the asters is in itself not sufficient to account for division of the cytoplasm.

referred to at page 215, finds that after treatment with magnesium chloride unfertilized sea-urchin eggs (*Arbacia*) may give rise to perfect *Pluteus* larvæ — a result which if well founded seems to place the new formation of true centrosomes beyond question.

Taken together, these researches give strong ground for the conclusion that true (*i.e.* physiological) centrosomes may arise *de novo* from either the cytoplasmic or the nuclear substance and may play the usual *rôle* (whatever that may be) in mitosis. If this conclusion be sustained by future research, we shall no longer be able to accept Van Beneden's and Boveri's conception of the centrosome as a persistent organ in the same sense as the nucleus; but on the other hand we shall have gained important ground for further inquiry into the nature and source of that power of division which is so characteristic of living things and upon which the law of genetic continuity rests.

Morphology of the Centrosome. — In its simplest form (Fig. 152, *A*) the centrosome appears under the highest powers as nothing more than a single granule of extraordinary minuteness which stains intensely with iron-hæmatoxylin, and can scarcely be distinguished from the cyto-microsomes except for the fact that it lies at the focus of the astral rays. In this form it always appears at the centre of the very young sperm-asters during fertilization (Figs. 97, 99), in the early phases of ordinary mitosis (Figs. 27, 32), and in some cases also in the resting cell, for example, in leucocytes and connective tissue corpuscles (Figs. 8, 49), where, however, it is often triple or quadruple. In the course of division the centrosome often increases in size and assumes a more complex form, becoming also surrounded by various structures involved in the aster-formation. The relation of these structures to the centrosome itself has not yet been fully cleared up and there is still much divergence of opinion regarding the cycle of changes through which the centrosome passes. It is, therefore, not yet possible to give a very consistent account of the centrosome, still less to frame a satisfactory morphological definition of it.

It is convenient to take up as a starting-point Boveri's ('88) account of the centrosomes in the egg of *Ascaris*, supplemented by Brauer's ('93) description of those in the spermatocytes of the same animal. During the early prophases of the first cleavage Boveri found the centrosome as a minute granule which steadily enlarges as the spindle forms, until shortly before the metaphase it becomes a rather large, well-defined sphere in the centre of which a minute *central granule* or *centriole* appears (Fig. 152, *B*, *C*). From this time onward the centrosome decreases in size until in the daughter-cells it is again reduced to a small granule which divides into two and goes through a similar cycle during the second cleavage and so on. The centrosome is at all stages surrounded by a clear zone ("Heller Hof") in which the astral rays are thinner and stain less deeply than farther out. Brauer's account is substantially the same, though no definite "Heller Hof" was found, and the astral rays were traced directly in to the boundary of the centrosome. He added, however, two important observations, viz. (1) that the central granule is visible at every period; and (2) *division of the centrosome is preceded by division of the central granule* (Fig. 148) — an observation recently extended by Boveri to the division of the egg-centrosome.[1] Van Beneden and Neyt ('87), on the other hand, gave a quite different account of the structures at the centre of the aster. The "corpuscule central" (usually assumed by later writers to be the centrosome), described as a "mass of granules," is surrounded by two well-defined astral zones, formed as modifications of the inner part of the aster, and constituting the "attraction-sphere." These are an inner "medullary zone," and an outer "cortical zone," each bounded by a very distinct layer of microsomes (Fig. 152, *F*).

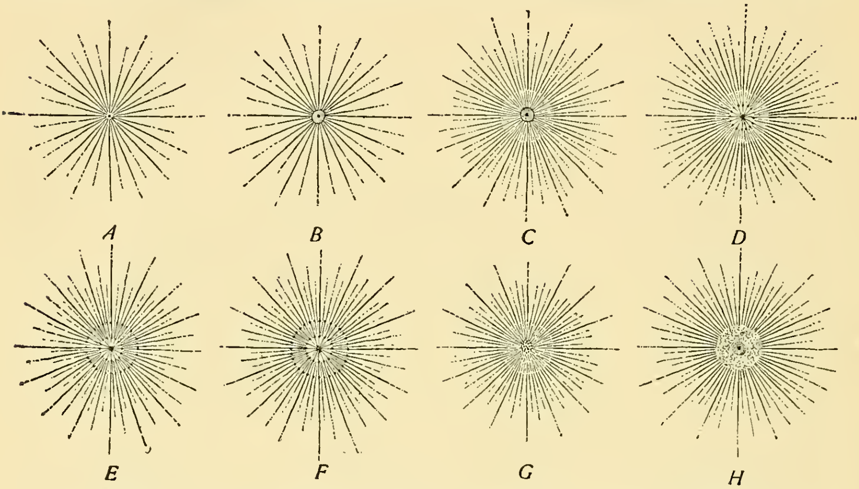

Fig. 152. — Diagrams illustrating various accounts of centrosome and aster.

A. Centrosome, a simple granule at the centre of the aster; *ex*. sperm-aster in various animals. *B*. "Centrosome," a sphere enclosing a central granule or centriole; *ex*. Brauer's account of spermatocytes of *Ascaris*. *C*. Like the last, but "centrosome" surrounded by a "Heller Hof"; *ex*. Boveri's account of the centrosome of the *Ascaris* egg. *D*. Central granule surrounded by a radial sphere ("centrosome") bounded by a microsome-circle, and lying in a "Heller Hof"; *ex*. polar spindles of *Thysanozoön*, Van der Stricht. *E*. Central granule ("centrosome") surrounded by medullary and cortical radial zones, each bounded by a microsome-circle; *ex*. polar spindle of *Unio*, Lillie. *F*. Van Beneden's representation of aster of the *Ascaris* egg; like the last, but the "corpuscule central" consisting of a group of granules. *G*. "Centrosome," a group of granules surrounded by a "Heller Hof"; *ex*. the echinoderm-egg. *H*. "Centrosome" (central granule) surrounded by a vague larger body lying in a reticulated centrosphere; *ex*. *Thalassema*. [GRIFFIN.]

---

[1] Reported by Fürst, '98, p. 111.

The discrepancy between these results on the part of the two pioneer investigators of the centrosome has led to great confusion in the terminology of the subject, which has not yet been fully cleared away. Many of the observers who followed Boveri (Flemming, Hermann, Van der Stricht, Heidenhain, etc.) found the centrosome, in various cells, as a much smaller body than he had described, often as a single or double minute granule, staining intensely with iron-hæmatoxylin. Heidenhain ('93, '94) and Drüner ('94, '95) found further that the asters in leucocytes and other forms often show several concentric circles of microsomes, and that the sphere bounded by the innermost circle often stains more deeply than the outer portions and may appear nearly or quite homogeneous (Fig. 156). To this sphere, with its contained central granule or granules Heidenhain applies the term *microcentrum* ('94, p. 463), while Kostanecki and Siedlecki suggest the term *microsphere* ('96, p. 217). Still later Kostanecki and Siedlecki ('97) found that even in *Ascaris*, as in other forms, sufficient extraction of the colour (iron-hæmatoxylin) reduces the centrosome to a minute granule to which the astral rays converge, and which is presumably identical with Boveri's "central granule." Heidenhain ('93, '94) found that in leucocytes the central granule is often double, triple, or even quadruple, while in giant-cells of certain kinds there are numerous deeply staining granules (Fig. 14). He therefore proposed to restrict the term *centrosome* to the individual granules, whatever be their number, applying the term *microcentrum* to the entire group ('94, p. 463).

With these facts in mind we can gain a clear view of the manner in which both the confusion of terminology and the contradiction of results has arisen. Brauer ('93) found in *Ascaris* (see above) that *division of the central granule precedes division of the "centrosome,"* and therefore suggested that only the former is equivalent to Van Beneden's "corpuscule central," while the body called "centrosome" by Boveri is really the medullary astral zone, the "Heller Hof" being the cortical zone. This is substantially the same conclusion reached by Heidenhain, Rawitz, Lenhossék, Kostanecki and Siedlecki, Erlanger, Van der Stricht, Lillie, and several others. The confusion of the subject is owing, on the one hand, to the fact that those who have accepted this conclusion continue to use the word *centrosome* in two quite different senses, on the other hand to the fact that the conclusion is itself repudiated by Boveri ('95), MacFarland ('97), and Fürst ('98).

As regards the terminology we find that most recent writers agree with Heidenhain, Kostanecki and Siedlecki, in restricting the word *centrosome* to the minute, deeply staining granules, whether one or more, at the centre of the aster. On the other hand, Brauer, Francotte, Van der Stricht, Meves, and others apply the term to the central granule or granules plus the surrounding sphere ("centrosome" of Boveri), which they regard as equivalent to the medullary zone of Van Beneden, the "corpuscule central" of the last-named author being identified with the central granule or "centriole" of Boveri, though the latter structure is considerably smaller than the former as described by Van Beneden.

The matter of fact turns largely on the question whether the astral rays traverse the larger sphere to the central granule. That such is the case in *Ascaris* is positively asserted by Kostanecki and Siedlecki, ('97) and as positively denied by Fürst ('98) with whose observations those of MacFarland ('97) on gasteropod-eggs agree. On the other hand, in the turbellarians the observations of Francotte ('97, '98) and Van der Stricht ('98, 1) seem to leave no doubt that the larger sphere ("centrosome"), here very sharply defined and staining deeply in iron-hæmatoxylin, is traversed by well-defined astral rays converging to the central corpuscle, and both these observers agree further that *both the corpuscle and the sphere divide to persist as the "centrosomes" of the daughter-cells* — a result in conformity with Van Beneden's conclusion in the case of *Ascaris*.

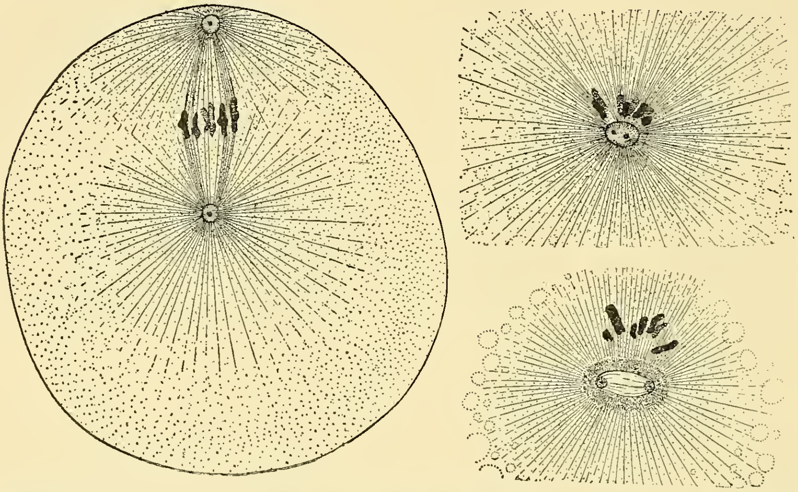

Fig. 153. — Structure of the centrosome in the polar asters of a gasteropod, *Diaulula*. [MACFARLAND.]

A. Mitotic figure, formation of first polar body. *B*. Inner aster at final anaphase; central granule double within the "centrosome." *C*. Elongation of old "centrosome" to form second polar spindle.

Lillie's valuable observations on the polar asters of *Unio* ('98) afford, I believe, conclusive evidence as to the nature of the sphere. In the earlier stages the aster has exactly the structure described by Van Beneden in *Ascaris*, except that the innermost body (*i.e.* the "corpuscule central") is a single minute granule. This is surrounded by typical medullary and cortical zones, through both of which the rays pass (Fig. 152, *E*, Fig. 154). The inner sphere, consisting of a dense and deeply staining substance, has at first a typical radiate structure and is bounded by a microsome-circle. In later stages (late anaphase) the central granule divides into two and afterward into four or more granules, of which, however, only one or two actually

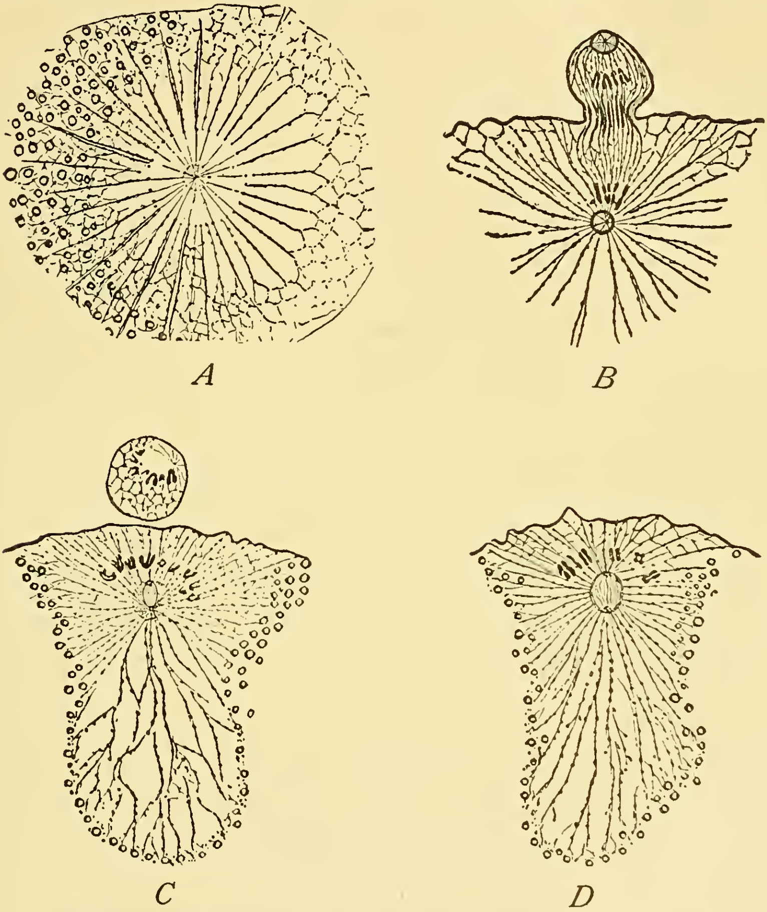

Fig. 154. — Centrosome and aster in the polar mitoses of *Unio*. [LILLIE.]

A. Aster of the first polar figure; central granule (centrosome) surrounded by medullary (entosphere) and cortical (ectosphere) zones. *B*. Late anaphase of second polar mitosis; radial entosphere bounded by continuous membrane. *C*. *D*. Prophases of second mitosis; formation of central spindle within and from the substance of the old entosphere.

persist. The inner sphere is now bounded by a definite membrane, and its radiate structure becomes obscure, the astral rays extending only to the boundary of the sphere, though a few rays persist within it (Fig. 154, *B*). It is clear from this that the inner sphere and central granule pass through phases that bridge the gap between Van Beneden's and Boveri's descriptions. Lillie's observations fully sustain the conclusion that the *central granule* (*"centriole" of Boveri*) *corresponds to the "corpuscule central" of Van Beneden, and the inner sphere* (*medullary zone*) *to Boveri's "centrosome."* A comparison of the polar aster of *Unio* with that of *Thysanozoön*, as described by Van der Stricht ('98), leaves hardly room for doubt that the cortical zone represents Boveri's "Heller Hof"; for in both forms the rays of the cortical zone are much thinner and lighter than the more peripheral portions, thus giving a clear zone, which in *Unio* is bounded by only a fairly definite microsome-circle and in *Thysanozoön* by none.

Lastly, we must recognize the justice of the view urged by Kostanecki, Griffin, Mead, Lillie, Coe, and others, that the term *centrosome* should be applied to the central granule and not to the sphere surrounding it (medullary zone), despite the fact that historically the word was first applied by Boveri to the latter structure. For in both *Diaulula* (MacFarland) and *Unio* (Lillie) the second polar spindle arises from the substance of the inner sphere, while the central granule, becoming double, gives rise to the centrosomes at its poles. By following Boveri's terminology, therefore, MacFarland is driven to the strange conclusion that the second polar spindle is nothing other than an enormously enlarged "centrosome" — a result little short of a *reductio ad absurdum* when we consider that in *Ascaris* the polar spindle arises by a direct transformation of the germinal vesicle (p. 277). The obvious interpretation is that the central granule is the only structure that should be called a centrosome, the surrounding sphere being a part of the aster, or rather of the attraction-sphere. Thus regarded, the origin of the spindle in *Diaulula* presents nothing anomalous and a similar interpretation may be placed on the polar spindles of *Ascaris* as described by Fürst ('98).[1]

---

[1] In echinoderms the concurrent results of Reinke ('95), Boveri ('95), myself ('96–'97), show that the "centrosome" is a well-defined sphere containing a large group (ten to twenty) of irregularly scattered, deeply staining granules. I have shown in this case that in the early prophases there is but one such granule, which then becomes double and finally multiple, forming a pluricorpuscular centrum (Fig. 52) not unlike that described by Heidenhain in giant-cells. Kostanecki, who asserts that the centrosome of echinoderms is a single granule ('96, 1, '96, 2, p. 248), has not sufficiently studied the later phases of mitosis. *Cf.* also Erlanger ('98). The centrosomes described in nerve cells by Lenhossék ('95) are apparently of somewhat similar type. Until the facts are more fully known the exact nature of these "centrosomes" remains an open question. Lillie's observations on *Unio* show that here, too (first polar spindle), the centrosome divides to form a considerable number of

The genesis of the concentric spheres surrounding the centrosome will be considered in the following section. We may here only emphasize the remarkable fact that the centres of the dividing system are bodies which are in many cases so small as to lie almost at the limits of microscopical vision, and which in the absence of the surrounding structures could not be distinguished from other protoplasmic granules. Full weight should be given to this fact in every estimate of the centrosome theory, and it is no less interesting in its bearing upon the corpuscular theory of protoplasm.

Watasé ('93, '94) made the very interesting suggestion that *the centrosome is itself nothing other than a microsome* of the same morphological nature as those of the astral rays and the general meshwork, differing from them only in size and in its peculiar powers.[1] Despite the vagueness of the word "microsome," which has no well-defined meaning, Watasé's suggestion is full of interest, indicating as it does that the centrosome is morphologically comparable to other elementary bodies existing in the cytoplasmic structure, and which, minute though they are, may have specific chemical and physiological properties.

An interesting hypothesis regarding the historical origin of centrosome is that of Bütschli ('91) and R. Hertwig ('92), who suggest that it may be a derivative of a body comparable with the micro-nucleus of Infusoria, which has lost its chromatin but retained the power of division; and the last-named author has suggested further that the so-called "archoplasmic loops" discovered by Platner in pulmonates may be remnants of the chromatic elements. A similar view has been advocated by Heidenhain ('93, '94) and Lauterborn ('96). Heidenhain regards central spindle and centrosomes as forming essentially a unit ("microcentrum") homologous with the micro-nucleus of the Infusoria, the centrodesmus (p. 79) representing a part of the original achromatic elements. The metazoan nucleus is compared to the protozoan macro-nucleus. The improbability of a direct derivation of the Metazoa from Infusoria, urged by Boveri ('95) and Hertwig ('96), has led Lauterborn ('96) to the view that the metazoan centrosome and nucleus are respectively derivatives of two equivalent nuclei, such as Schaudinn ('95) describes in *Amœba binucleata*, the "Nebenkörper" of *Paramœba* (*cf.* p. 94), being regarded as an intermediate step, and the micro-nucleus of Infusoria a side-branch. R. Hertwig ('96), on the other hand, regards the metazoön centrosome as a derivative of an intra-nuclear body such as the "nucleolo-centrosome" of *Euglena* (p. 91), which has itself arisen through a condensation of the general achromatic substance. With this view Calkins ('98), on the whole, agrees; but he regards it as probable that the "nucleolo-centrosome"

---

granules of which one or two remain as the persistent centrosome, while others are converted into microsomes or other cytoplasmic structures. It is probable that something similar occurs in the echinoderms.

[1] The microsome is conceived, if I understand Watasé rightly, not as a permanent morphological body, but as a temporary varicosity of the thread, which may lose its identity in the thread and reappear when the thread contracts. The centrosome is in like manner not a permanent organ like the nucleus, but a temporary body formed at the focus of the astral rays. Once formed, however, it may long persist even after disappearance of the aster, and serve as a centre of formation for a new aster.

of *Euglena* and *Amœba* and the sphere of *Noctiluca* and *Paramœba* are to be compared with the attraction-sphere, while the centrosome may have had a different origin.

It appears to me that none of these views rests upon a very substantial basis, and they must be taken rather as suggestions for further work than as well-grounded conclusions.

F. The Archoplasmic Structures

1. *Hypothesis of Fibrillar Persistence*

The asters and attraction-spheres have a special interest for the study of cell-organs; for they are structures that may divide and persist from cell to cell or may lose their identity and re-form in successive cell-generations, and we may here trace with the greatest clearness the origin of a cell-organ by differentiation out of the structural basis. Two sharply opposing views of these structures have been held, represented among the earlier observers on the one hand by Boveri, on the other by Bütschli, Klein, Van Beneden, and Carnoy. The latter observers held that the astral rays and spindle-fibres, and hence the attraction-sphere, arise through a morphological rearrangement of the preëxisting protoplasmic meshwork, under the influence of the centrosome. This view, which may be traced back to the early work of Fol ('73) and Auerbach ('74), was first clearly formulated by Bütschli ('76), who regarded the aster as the optical expression of a peculiar physico-chemical alteration of the protoplasm primarily caused by diffusion-currents converging to the central area of the aster.[1] An essentially similar view is maintained in Bütschli's recent great work on protoplasm,[2] the astral "rays" being regarded as nothing more than the meshes of an alveolar structure arranged radially about the centrosomes (Fig. 10, *B*). The fibrous appearance of the astral rays is an optical illusion, for they are not fibres, but flat lamellæ forming the walls of elongated closed chambers. This view has recently been urged, especially by Erlanger ('97, 4, etc.), who sees in all forms of asters and spindles nothing more than a modified alveolar structure.

The same general conception of the aster is adopted by most of those who accept the fibrillar or reticular theory of protoplasm, the astral rays and spindle-fibres being regarded as actual fibres forming part of the general network. One of the first to frame such a conception was Klein ('78), who regarded the aster as due to "a radial arrangement of what corresponds to the cell-substance," the latter being described as having a fibrillar character.[1] The same view is advocated by Van Beneden in 1883. With Klein, Heitzman, and Frommann he accepted the view that the intra-nuclear and extra-nuclear networks were organically connected, and maintained that the spindle-fibres arose from both.[2] "The star-like rays of the asters are nothing but local differentiations of the protoplasmic network.[3] . . . In my opinion the appearance of the attraction-spheres, the polar corpuscle (centrosome), and the rays extending from it, including the achromatic fibrils of the spindle, are the result of the appearance in the egg-protoplasm of two centres of attraction comparable to two magnetic poles. This appearance leads to a regular arrangement of the reticulated protoplasmic fibrils and of the achromatic nuclear substance with relation to the centres, in the same way that a magnet produces the stellate arrangement of iron filings."[4]

---

[1] For a very careful review of the early views on this subject, see Mark, *Limax*, 1881.

[2] '92, 2, pp. 158–169.

This view is further developed in Van Beneden's second paper, published jointly with Neyt ('87). "The spindle is nothing but a differentiated portion of the asters."[5] The aster is a "radial structure of the cell-protoplasm, whence results the image designated by the name of aster."[6] The operations of cell-division are carried out through the "contractility of the fibrillæ of the cell-protoplasm and their arrangement in a kind of radial muscular system composed of antagonizing groups."[7]

An essentially similar view of the achromatic figure has been advocated by many later workers. Numerous observers, such as Rabl, Flemming, Carnoy, Watasé, Wilson, Reinke, etc., have observed that the astral fibres branch out peripherally into the general meshwork and become perfectly continuous with its meshes, and tracing the development of the aster, step by step, have concluded that the rays arise by a direct progressive modification of the preexisting structure. The most extreme development of this view is contained in the works of Heidenhain ('93, '94), Bühler ('95), Kostanecki and Siedlecki ('97), which are, however, only a development of the ideas suggested by Rabl in a brief paper published several years before. Rabl ('89, 2) suggested that neither spindle-fibres nor astral rays really lose their identity in the resting cell, being only modified in form to constitute the mitome or filar substance (meshwork), but still being centred in the centrosome. Fission of the centrosome is followed by that of the latent spindle-fibres (forming the linin-network); hence each chromosome is connected by pairs of daughter-fibres with the respective centrosomes. Heidenhain, adopting the first of these assumptions, builds upon it an elaborate theory of cell-polarity and cell-division already considered in part at pages 103–105. Sometimes the astral rays ("organic radii") retain their radial arrangement throughout the life of the cell (leucocytes, Fig. 49); more commonly they are disguised and lost to view in the cytoplasmic meshwork. All, however, are equal in length and in tension — assumptions based on the one hand on the occurrence of concentric circles of microsomes in the aster, on the other hand on the analogy of the artificial model described at page 104. Bühler ('95) and Kostanecki and Siedlecki ('97) likewise unreservedly accept the view that besides the centrosome the entire system of "organic radii," including astral rays, mantle-fibres, and central spindle-fibres, persists in the resting cell in modified form, and is centred in the centrosome. Kostanecki finally ('97) takes the last step, logically necessitated by the foregoing conclusion, and apparently supported also by the crossing of the astral rays opposite the equator of the spindle and the relations of their peripheral ends, concluding that the monocentric astral system is converted into the dicentric system (amphiaster) by *longitudinal fission of the rays*.[1] Thus the entire mitome of the mother-cell divides into equal halves for daughter-cells; and since the radii consist of microsomes, each of these must likewise divide into two.[2]

---

[1] It is interesting to note that in the same place Klein anticipated the theory of fibrillar contractility, both the nuclear and the cytoplasmic reticulum being regarded as contractile (*l.c.*, p. 417).

[2] '83, p. 592.

[3] '83, p. 576.

[4] '83, p. 550.

[5] '87, p. 263.

[6] *l.c.*, p. 275.

[7] *l.c.*, p. 280.

Could this tempting hypothesis be established, Roux's interpretation of nuclear division (p. 224) could be extended also to the cytoplasm; and the aster- and amphiaster-formation, with the spireme-formation, might be conceived as a device for the meristic division of the entire cell-substance — a result which would place upon a substantial basis the general corpuscular theory of protoplasm. Unfortunately, however, the hypothesis rests upon a very insecure foundation: first, because it is based solely upon the fibrillar theory of protoplasm; second, because of the very incomplete direct evidence of such a splitting of the rays; third, because there is very strong evidence that in many cases the old astral rays wholly disappear, to be replaced by new ones.[3] We may best consider this adverse evidence in connection with a general account of the opposing archoplasm-hypothesis.

2. *The Archoplasm Hypothesis*

Entirely opposed to the foregoing conception are the views of Boveri and his followers, the starting point of which is given by

---

[1] '97, p. 680.

[2] This view had been definitely stated also by O. Schultze in 1890.

[3] There is, however, no doubt that the aster as a whole does, in some cases, divide into two — for instance, in the echinoderm-egg, Fig. 95.

Boveri's celebrated archoplasm-hypothesis. Boveri has from the first maintained that the amphiastral fibres are quite distinct from the general cell-meshwork. In his earlier papers he maintained ('88, 2) that the attraction-sphere of the resting cell is composed of a distinct substance, "*archoplasm*," consisting of granules or microsomes aggregated about the centrosome as the result of an attractive force exerted by the latter. From the material of the attraction-sphere arises the entire achromatic figure, including both the spindle-fibres and the astral rays, and these have nothing to do with the general reticulum of the cell. They grow out from the attraction-sphere into the reticulum as the roots of a plant grow into the soil, and at the close of mitosis are again withdrawn into the central mass, breaking up into granules meanwhile, so that each daughter-cell receives one-half of the entire archoplasmic material of the parent-cell. Boveri was further inclined to believe that the individual granules or archoplasmic microsomes were "independent structures, not the nodal points of a general network," and that the archoplasmic rays arose by the arrangement of these granules in rows without loss of their identity.[1] In a later paper on the sea-urchin this view underwent a considerable modification through the admission that the archoplasm may not preexist as formed material, but that the rays and fibres may be a new formation, crystallizing, as it were, out of the protoplasm about the centrosome as a centre, but having no organic relation with the general reticulum; though Boveri still held open the possibility that the archoplasm might preëxist in the form of a specific homogeneous substance distributed through the cell, though not ordinarily demonstrable by reagents.[2] In this form the archoplasm-theory approaches very nearly that of Strasburger, described below.

There are three orders of facts that tell in favour of Boveri's modified theory: first, the existence of persistent archoplasm-masses or attraction-spheres from which the amphiasters arise; second, the origin of amphiasters in alveolar protoplasm; and, third, the increasing number of accounts asserting the replacement of the old asters by others of quite new formation. In at least one case, namely, that of *Noctiluca*, the entire achromatic figure is formed from a permanent attraction-sphere lying outside the nucleus and perfectly distinct from the general cell-meshwork.[3] Other cases of this kind are very rare, and in most cases the attraction-sphere sooner or later disintegrates,[4] but in the formation of the spermatozoa we have many examples of archoplasmic masses (Nebenkern, attraction-sphere, idiozome), which apparently consist of a specific substance having a special relation to the achromatic figure.

---

[1] '88, 2, p. 80.

[2] '95, 2, p. 40.

[3] Ishikawa, '94, '98; Calkins, '98, 2.

[4] *Cf.* p. 323.

The amphiastral formation in alveolar protoplasm gives very clear evidence against the theory of fibrillar persistence. Here the fibrillar rays can be seen growing out through the walls of the alveoli[1] quite distinct from, though embedded in, them. At the close of mitosis every trace of the fibrillar formation may disappear, *e.g.* in echinoderm-eggs after formation of the polar bodies, the protoplasm retaining only a typical alveolar structure.

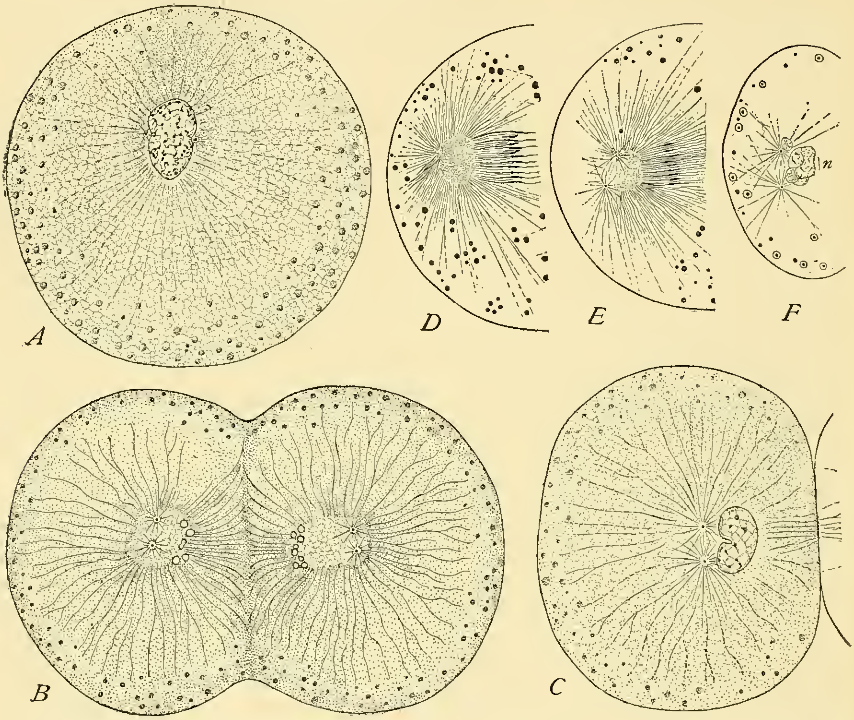

Fig. 155.—Stages in the first cleavage of the egg in *Cerebratulus* (*A–C*, Coe) and *Thalassema* (*D–F*, Griffin).

A. First appearance of the cleavage-centrosome at the poles of the fused germ-nuclei; cleavage-asters forming within the degenerating sperm-asters. *B.* Final anaphase of first cleavage, showing persistent centrosomes and new asters forming. *C.* Immediately after division. *D–F.* Three stages of the late anaphase in *Thalassema*, showing formation of new asters within the old. (*Cf.* Fig. 99.)

The strongest evidence against fibrillar persistence is, however, given by recent studies on mitosis, showing on the one hand that the new astral centres do not coincide with the old ones, on the other that the old rays degenerate *in situ*, to be replaced by new ones. Aside from many earlier observers, who believed the entire aster to disappear at the close of mitosis, the first to assert the wholly new formation of the rays was Drüner, who maintained in the case of the mitosis of salamander testis-cells, that "not a single fibre of the astral system of the mother-cell is carried over unchanged into the organism of the daughter-cell" ('95, p. 309). The same conclusion was soon afterward supported by Braus ('95) in the case of the cleavage-mitoses of *Triton*. The most convincing evidence of this fact has been given by studies on the maturation and fertilization of the egg by Griffin ('96, '99), MacFarland ('97), Lillie ('99), and Coe ('99), all of whom find that the new astral centres, arising by division of the centrosome, move away from the old position, *to which, however, the old rays still converge while the new asters are independently forming* (Fig. 155). This is shown with especial clearness in the egg of *Cerebratulus* (Coe), where the peripheral portions of the old asters persist until the new amphiaster is completely formed. This observation seems conclusively to overturn Kostanecki's hypothesis of the persistence and division of the rays, and together with the work of MacFarland gives a very strong support to Boveri's later view.

---

[1] *Cf.* Reinke ('95), Wilson ('99).

It still remains an open question whether the rays actually arise from the substance of the centrosome, from a specific surrounding archoplasm, or by differentiation out of the general substance of the meshwork. The first of these possibilities has been urged in a very interesting way by Watasé ('94), who believes that the centrosome "spins out the cytoplasmic filaments"[1] of the spindle and aster, and that ordinary microsomes may in like manner spin out the fibrillæ of ordinary cytoplasmic networks.[2] This view is sustained by the mode of origin of the axial filament in the spermatozoa and that of the cilia in plant spermatozoids. It is, on the other hand, opposed by the almost infinitesimal bulk of the centrosome as compared with that of the aster that may form about it, and by the formation of the spindles in higher plants in the apparent absence of centrosomes. On the whole, the facts do not seem at present to warrant the acceptance of Watasé's ingenious hypothesis, and the most probable view is that of Drüner and Boveri, that the rays are differentiated out of the walls of the meshwork. In cases where the protoplasm is reticular or fibrillar the differentiation of the rays may be indistinguishable from a mere rearrangement of the thread-work; in alveolar protoplasm they may be seen as new formations, while in either case the material of the old aster may be more or less directly utilized in the building of the new. The feature common to all is the periodic activity either of the centre itself or of the surrounding protoplasm, and the coincidence or non-coincidence of the new aster with the old is apparently a secondary matter.

---

[1] *l.c.*, p. 283.

[2] See the same paper for a suggestive comparison of the astral fibrillæ to muscle-fibres

In its original form the archoplasm hypothesis, as stated by Boveri, was developed with reference only to the material of the spindle-fibres and astral rays. Later writers have greatly extended the conception on the basis of Boveri's earlier view that archoplasm is a specific form of protoplasm, possessing specially active properties. Strasburger ('92–'98), whose views have already been considered in part, believes the protoplasm to consist of, or to show a tendency to differentiate itself into, two distinct substances, namely, a specially active fibrillar *kinoplasm* and a less active alveolar *trophoplasm*. The former gives rise to the mitotic fibrillæ, constitutes the peripheral cell layer, or *Hautschicht*, from which the membrane arises, forms the substance of the centrosomes, and gives origin to the contractile substance of cilia and flagella. The kinoplasm is thus mainly concerned with the motor phenomena of the cell, the trophoplasm with those of nutrition; and this physiological difference is morphologically expressed in the fact that the former has in general a fibrillar structure, the latter an alveolar. Beyond this the two forms of protoplasm show a difference of staining-reaction, the kinoplasmic fibrillæ staining deeply with gentian-violet and iron-hæmatoxylin, while the trophoplasm is but slightly stained.

Prenant ('98, '99) still further extends the hypothesis, adopting the view that the "ergastoplasmic" (Garnier) fibrillæ of gland-cells[1] are equivalent to the kinoplasmic or archoplasmic fibrillæ of the mitotic figure, and to the fibrillæ of nerve- and muscle-fibres as well. He is thus led to the conception of a dominating or "superior" cytoplasm (including "archoplasm," "kinoplasm," "ergastoplasm"), which arises by differentiation out of the general cytoplasm, plays the leading *rôle* in the elaboration of active cell-elements ("cytosomes"), such as mitotic, neural, and glandular fibrillæ, and finally, its *rôle* accomplished, may disappear. Under the same category with the foregoing structures are placed the centrosome, attraction-sphere, mid-body, idiozome, Nebenkern, and yolk-nucleus.

Such a generous expansion of the archoplasm-hypothesis brings it perilously near to a *reductio ad absurdum;* for the step is not a great one to the identification of the "superior protoplasm" with the active cell-substance in general, which would render the whole hypothesis superfluous. Physiologically, we can draw no definite line of demarcation between the more and the less active protoplasmic elements, and it may further be doubted whether such a boundary exists even between the latter and the metaplasmic substances.[2] It is further quite unjustifiable to infer physiological likeness from similarity in staining-reaction[3] or in fibrillar structure. For these reasons the hypothesis of "superior protoplasm" seems one of doubtful utility.

---

[1] *Cf.* the pancreas, p. 44.

[2] *Cf.* p. 29.

[3] *Cf.* p. 335.

In its more restricted form, however, the archoplasm or kinoplasm hypothesis is of high interest as indicating a common element in the origin and function of the mitotic fibrillæ, the centrosome and mid-body, and the contractile substances of cilia, flagella, and muscle-fibres. The main interest of the hypothesis seems to me to lie in the definite genetic relations that have been traced between the archoplasmic structures of successive cell-generations (as is most clearly shown in the phenomena of maturation and fertilization). It has been pointed out at various places in the preceding chapters[1] how many apparently contradictory phenomena in cell-division, fertilization, and related processes can be brought into relation with one another under the assumption of a specific substance, carried by the centrosome or less definitely localized, which gives the stimulus to division, which is concerned in the formation of the mitotic figure and of contractile elements, and which may be transmitted from cell to cell without loss of its specific character. There seems, however, to be clear evidence that such substance (or substances), if it exists, is not to be regarded as being necessarily a permanent constituent of the cell, but only as a phase, more or less persistent, in the general metabolic transformation of the cell-substance.[2]

3. *The Attraction-sphere*

As originally used by Van Beneden[3] the term *attraction-sphere* was applied (in *Ascaris*) to the central mass of the aster surrounding the "corpuscule central" and consisting of medullary and cortical zones, as already described (p. 310). The cortical zone is bounded by a distinct circle of microsomes from which the astral rays proceed; and at the close of cell-division the rays were stated to fade away, leaving only the attraction-sphere, which, like the centrosome, was regarded as a permanent cell-organ. Later researches have conclusively shown that the attraction-sphere cannot be regarded as a permanent organ, since in many cases it disintegrates and disappears. This occurs, for example, in the early prophases of mitosis in the testis-cells of the salamander,[4] where the sphere breaks up and scatters through the cell as the new amphiaster forms (Fig. 27). A very interesting case of this kind occurs in the cleavage of the ovum in *Crepidula*, as described by Conklin ('99). The spheres here persist for a considerable period after division (Fig. 192), but have no direct relation to those of the ensuing division, finally disappearing *in situ*. The new spheres are formed about the centrosomes, which Conklin believes to migrate out of the old spheres (somewhat as occurs in the spermatid, p. 167) to their new position. The interesting point here is that the old sphere takes up such a position as to pass entirely into *one* of the grand-daughter-cells, while the new sphere-substance is equally distributed between them and in its turn passes into one of the cells of the ensuing division.[1]

---

[1] *Cf.* pp. 111, 215.

[2] *Cf.* p. 171.

[3] '83, p. 548.

[4] Drüner, '95, Rawitz, '96, Meves, '96.

In *Crepidula*, as in *Ascaris*, the attraction-sphere represents only the central part (centrosphere) of the aster. In some cases, however, *e.g.* in leucocytes, the entire aster may persist, and the term *attraction-sphere* has by some authors been applied to the whole structure. Later workers have proposed different terminologies, which are at present in a state of complete confusion. Fol ('91) proposed to call the centrosome the *astrocentre*, and the spherical mass surrounding it (attraction-sphere of Van Beneden) the *astrosphere*. Strasburger accepted the latter term but proposed the new word *centrosphere* for the astrosphere and the centrosome taken together.[2] A new complication was introduced by Boveri ('95), who applied the word "astrosphere" to the *entire aster* exclusive of the centrosome, in which sense the phrase "astral sphere" had been employed by Mark in 1881. The word "astrosphere" has therefore a double meaning and would better be abandoned in favour of Strasburger's convenient term *centrosphere*, which may be understood as equivalent to the "astrosphere" of Fol.

Besides these terms we have Heidenhain's *microcentrum* (p. 311), equivalent to the centrosome or group of centrosomes at the centre of the aster, with its surrounding sphere;[3] Kostanecki's and Siedlecki's *microsphere*, applied to the central region of the aster surrounding the centrosome whether bounded by a distinct microsome-circle or not;[4] Erlanger's *centroplasm*, equivalent to microsphere;[5] Ziegler's *ectosphere* and *entosphere*, applied to the cortical and medullary zones respectively; and Meves's *idiozome*, applied to the "attraction-sphere" of the spermatids.[6] This profusion of technical terms has arisen through the desire to avoid ambiguity in the use of the term "attraction-sphere," which, like the word "Nebenkern" (p. 163), has been applied to bodies of quite different origin and fate. If we adhere to Van Beneden's original use of the term it must be confined to the body surrounding the centrosome, forming a part of, or directly derived from, an aster, and giving rise wholly or in part to the succeeding aster. Meves ('96), Rawitz ('96), Erlanger ('97, 2), and others have, however, clearly shown that the "attraction-sphere" surrounding the centrosome (in testis-cells) may not only contain other material derived from the cytoplasm, *e.g.* the "centrodeutoplasm" of Erlanger, but may take no direct part in the succeeding aster-formation, disintegrating and scattering through the cell as the new aster forms (Fig. 27). In other cases a sphere closely simulating an attraction-sphere may arise in the cytoplasm without apparent relation to the centrosomes or to the preceding aster, *e.g.* the yolk-nucleus or the sphere from which the acrosome arises in mammalian spermatogenesis.[1] To call such structures "attraction-spheres" or "archoplasm-masses" is to beg an important question; and in all such doubtful cases the simple word *sphere* should be used.[2] In case of the aster itself we may, for descriptive purposes, employ Strasburger's convenient and non-committal term *centrosphere*, to designate in a somewhat vague and general way the central mass of the aster surrounding the centrosome, leaving its exact relation to Van Beneden's attraction-sphere to be determined in each individual case. Where the centrosphere shows two concentric zones (medullary and cortical), they may be well designated with Ziegler as *entosphere* ("centrosome" of Boveri) and *ectosphere*.

---

[1] *Cf.* p. 424.

[2] '92, p. 5.

[3] '94, p. 463.

[4] '96, p. 217.

[5] '96, 3, p. 8.

[6] '97, 4, p. 315.

As regards the structure of the centrosphere, two well-marked types have been described. In one of these, described by Van Beneden in *Ascaris*, by Heidenhain in leucocytes, by Drüner and Braus in dividing cells of Amphibia, and by Francotte, Van der Stricht, Lillie, Kostanecki, and others, in various segmenting eggs, the centrosphere has a radiate structure, being traversed by rays which stretch between the centrosome and the peripheral microsome-circle (Fig. 152, *D*, *E*, *F*), when the latter exists. In the other form, described by Vejdovský in the eggs of *Rhynchelmis*, by Solger and Zimmermann in pigment-cells, by myself in *Nereis*, by Rückert in *Cyclops*, by Mead in *Chætopterus*, Griffin in *Thalassema*, Coe in *Cerebratulus*, Gardiner in *Polychœrus*, and many others, the centrosphere has a non-radial reticular or vesicular structure, in which the centrosomes lie (Figs. 152, *H*, 155). Kostanecki and others have endeavoured to show that such structures are artifacts, insisting that in perfectly fixed material the astral rays always traverse the centrosphere to the centrosome. This interpretation is, however, contradicted by the fact that the new asters developing in the centrospheres during the anaphases and telophases of such forms as *Thalassema* or *Cerebratulus* (Figs. 99, 155) show perfect fixation of the rays. The reticular centrosphere almost certainly arises as a normal differentiation of the interior of the aster, which, as Griffin ('96) has suggested, probably marks the beginning of the degeneration of the whole astral apparatus, to make way for the newly developing system.

The radial centrosphere is in *Ascaris* divided into cortical and medullary zones, as already described (p. 310), the aster being bounded by a distinct circle of microsomes. The true interpretation of these zones was given through Heidenhain's beautiful studies on the asters in leucocytes, and the still more thorough later work of Drüner on the spermatocyte-divisions of the salamander. In leucocytes (Fig. 49) the large persistent aster has at its centre a well-marked radial sphere bounded by a circle of microsomes, as described by Van Beneden, but without division into cortical and medullary zones. The astral rays, however, show indications of other circles of microsomes lying outside the centrosphere. Drüner found that a whole series of such concentric circles might exist (in the cell shown in Fig. 156 no less than nine), but that the innermost two are often especially distinct, so as to mark off a centrosphere composed of a medullary and a cortical zone precisely as described by Van Beneden. These observations show conclusively that the centrosphere of the radial type is merely the innermost portion of the aster, which acquires a boundary through the especial development of a ring of microsomes, or otherwise, and which often further acquires an intense staining-capacity so as to appear like a centrosome (p. 313). In *Thysanozoön* (Van der Stricht) only a single ring of microsomes exists, and this lies at the boundary between the medullary and cortical zones (Fig. 152, *D*), the latter differing from the outer region only in the greater delicacy of the rays and their lack of staining-capacity, thus producing a "Heller Hof." In other cases, no "microsome-circles" exist; but even here a clear zone often surrounds the centrosome (*e.g.* in *Physa*, *t.* Kostanecki and Wierzejski), like that seen in the cortical zone of *Thysanozoön.*

---

[1] *Cf.* p. 170.

[2] *Cf.* Lenhossék, '98.

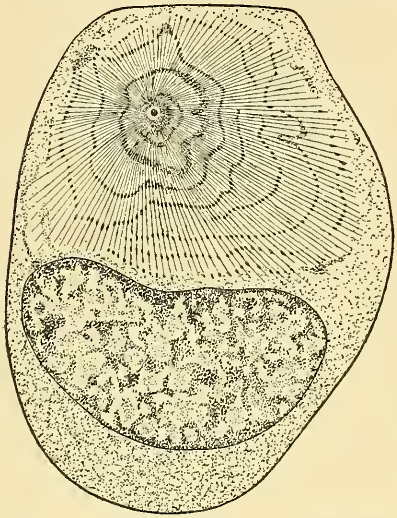

Fig. 156. — Spermatogonium of salamander. [DRÜNER.]

The nucleus lies below. Above is the enormous aster, the centrosome at its centre, its rays showing indications of nine concentric circles of microsomes. The area within the second circle probably represents the "attraction-sphere" of Van Beneden.

There are some observations indicating that the entosphere (medullary zone) may be directly derived from the centrosome (central granule). This is the conclusion reached by Lillie in the case of *Unio* referred to above, where, during the prophases of the second polar spindle, the central granule enlarges and breaks up into a group of granules from which the new entosphere is formed. Van der Stricht ('98) reaches a similar conclusion in case of the first polar spindle of *Thysanozoön.* We may perhaps give the same interpretation to the large pluricorpuscular centrum of echinoderms (p. 314). This observation may be used in support of the probability that the astral rays may be actually derived from the centrosome (p. 321); but Lillie finds in some cases that in the same mitosis the entosphere is formed by a different process, arising by a differentiation of the cytoplasm around the central granule. The former case, therefore, may be interpreted to mean simply that the centrosome may give rise to other cytoplasmic elements (as has already been shown in the formation of the spermatozoön, p. 172), the material of which may then contribute either directly or indirectly to the building of the aster; and the facts do not come into collision with the view that the astral rays are in general formed from the cytoplasmic substance.

G. Summary and Conclusion

A minute analysis of the various parts of the cell leads to the conclusion that all cell-organs, whether temporary or "permanent," are local differentiations of a common structural basis. Temporary organs, such as cilia or pseudopodia, are formed out of this basis, persist for a time, and finally merge their identity in the common basis again. Permanent organs, such as the nucleus or plastids, are constant areas in the same basis, which never are formed *de novo*, but arise by the division of preëxisting areas of the same kind. These two extremes are, however, connected by various intermediate gradations, examples of which are the contractile vacuoles of Protozoa, which belong to the category of temporary organs, yet in many cases are handed on from one cell to another by fission, and the attraction-spheres and asters, which may either persist from cell to cell or disappear and re-form about the centrosome. There is now considerable evidence that the centrosome itself may in some cases have the character of a permanent organ, in others may disappear and re-form like the asters.

The facts point toward the conclusion, which has been especially urged by De Vries and Wiesner, that the power of division, not only of the cell-organs, but also of the cell as a whole, may have its root in a like power on the part of more elementary masses or units of which the structural basis is itself built, *the degree of permanence in the cell-organs depending on the degree of cohesion manifested by these elementary bodies.* If such bodies exist, they must, however, in their primary form, lie beyond the present limits of the microscope, the visible structures arising by their enlargement or aggregation. The cell, therefore, cannot be regarded as a colony of "granules" or other gross morphological elements. The phenomena of cell-division show, however, that the dividing substance tends to differentiate itself into several orders of visible morphological aggregates, as is most clearly shown in the nuclear substance. Here the highest term is the plurivalent chromosome, the lowest the smallest visible dividing basichromatin-grains, while the intermediate terms are formed by the successive aggregation of these to form the chromatin-granules of which the dividing chromosomes consist. Whether any or all of these bodies are "individuals" is a question of words. The facts point, however, to the conclusion that at the bottom of the series there must be masses that cannot be further split up without loss of their characteristic properties, and which form the elementary morphological units of the nucleus.

In case of the cytoplasm the evidence is far less satisfactory. Could Rabl's theory of fibrillar persistence, as developed by Heidenhain and Kostanecki, be established, we should indeed have almost a demonstration of panmeristic division in the cytoplasm. At present, however, the facts do not admit the acceptance of that theory, and the division of the visible cytoplasmic granules must remain a quite open question. Yet we should remember that the dividing plastids of plant-cells are often very minute, and that in the centrosome we have a body, no larger in many cases than a "microsome," which is positively known to be in some cases a persistent morphological element, having the power of growth, division, and persistence in the daughter-cells. Probably these powers of the centrosome would never have been discovered were it not that its staining-capacity renders it conspicuous and its position at the focus of the astral rays isolates it for observation. When we consider the analogy between the centrosome and the basichromatin-grains, when we recall the evidence that the latter graduate into the oxychromatin-granules, and these in turn into the cytomicrosomes, we must admit that Brücke's cautious suggestion that the whole cell might be a congeries of self-propagating units of a lower order is sufficiently supported by fact to constitute a legitimate working hypothesis.

LITERATURE. VI[1]

Van Beneden, E. — (See List IV.)

Van Beneden and Julin. — La segmentation chez les Ascidiens et ses rapports avec l'organisation de la larve: *Arch. Biol.*, V. 1884.

Boveri, Th. — Zellenstudien. (See List IV.)

Brücke, C. — Die Elementarorganismen: *Wiener Sitz.-Ber.*, XLIV. 1861.

Bütschli, O. — Protoplasma. (See List I.)

Delage, Yves. — La structure du protoplasma, et les théories sur l'hérédité. *Paris*, 1895.

Häcker, V. — Über den heutigen Stand der Centrosomenfrage: *Verh. d. deutsch. Zoöl. Ges.* 1894.

Heidenhain, M. — (See List I.)

Herla, V. — Étude des variations de la mitose chez l'ascaride megalocéphale: *Arch. Biol.*, XIII. 1893.

---

[1] See also Literature, I., II., IV., V.

Morgan, T. H. — The Action of Salt-solutions on the Fertilized and Unfertilized Eggs of Arbacia and Other Animals. *Arch. Entw.*, VIII. 3. 1898.

Kostanecki, K. — Ueber die Bedeutung der Polstrahung während der Mitose. *Arch. mik. Anat.*, XLIX. 1897.

Nussbaum, M. — Über die Teilbarkeit der lebendigen Materie: *Arch. mik. Anat.*, XXVI. 1886.

Prenant, A. — Sur le protoplasma supérieure (archiplasme, kinoplasme, ergastroplasme): *Journ. Anat. et Phys.*, XXIV.-V. 1898–99. (Full Literature-lists.)

Rabl, C. — Über Zellteilung: *Morph. Jahrb.*, X. 1885. *Anat. Anzeiger*, IV. 1889.

Rückert, J. — (See List IV.)

De Vries, H. — Intracelluläre Pangenesis: *Jena*. 1889.

Watasé, S. — Homology of the Centrosome: *Journ. Morph.*, VIII. 2. 1893.

Id. — On the Nature of Cell-organization: *Woods Holl Biol. Lectures.* 1893.

Wiesner, J. — Die Elementarstruktur und das Wachstum der lebenden Substanz: *Wien*, 1892.

Wilson, Edm. B. — Archoplasm, Centrosome, and Chromatin in the Sea-urchin Egg: *Journ. Morph.*, Vol. XI. 1895.

CHAPTER VII

SOME ASPECTS OF CELL-CHEMISTRY AND CELL-PHYSIOLOGY

"Les phénomènes fonctionnels ou de dépense vitale *auraient donc leur siège dans le protoplasme cellulaire.*

"Le noyau est un appareil de *synthèse organique, l'instrument de la production, le germe de la cellule.*" CLAUDE BERNARD.[1]

I

A. CHEMICAL RELATIONS OF NUCLEUS AND CYTOPLASM

It is no part of the purpose of this work to give even a sketch of general cell-chemistry. I shall only attempt to consider certain questions that bear directly upon the functional relations of nucleus and cytoplasm and are of especial interest in relation to the process of nutrition and through it to the problems of development. It has often been pointed out that we know little or nothing of the chemical conditions existing in living protoplasm, since every attempt to examine them by precise methods necessarily kills the protoplasm. We must, therefore, in the main rest content with inferences based upon the chemical behaviour of dead cells. But even here investigation is beset with difficulties, since it is in most cases impossible to isolate the various parts of the cell for accurate chemical analysis, and we are obliged to rely largely on the less precise method of observing with the microscope the visible effects of dyes and other reagents. This difficulty is increased by the fact that both cytoplasm and karyoplasm are not simple chemical compounds, but mixtures of many complex substances; and both, moreover, undergo periodic changes of a complicated character which differ very widely in different kinds of cells. Our knowledge is, therefore, still fragmentary, and we have as yet scarcely passed the threshold of a subject which belongs largely to the cytology of the future.

It has been shown in the foregoing chapter that all the parts of the cell arise as local differentiations of a general protoplasmic basis. Despite the difficulties of chemical analysis referred to above, it has been determined with certainty that some at least of these organs are the seat of specific chemical change; just as is the case in the various organs and tissues of the organism at large. Thus, the nucleus is characterized by the presence of nuclein (chromatin) which has been proved by chemical analysis to differ widely from the cytoplasmic substances,[1] while the various forms of plastids are centres for the formation of chlorophyll, starch, or pigment. These facts give ground for the conclusion that the morphological differentiation of cell-organs is in general accompanied by underlying chemical specializations which are themselves the expression of differences of metabolic activity; and these relations, imperfectly comprehended as they are, are of fundamental importance to the student of development.

---

[1] *Leçons sur les phénomènes de la vie*, I., 1878, p. 198.

1. *The Proteids and their Allies*

The most important chemical compounds found in the cell are the group of *protein substances*, and there is every reason to believe that these form the principal basis of living protoplasm in all of its forms. These substances are complex compounds of carbon, hydrogen, nitrogen, and oxygen, often containing a small percentage of sulphur, and in some cases also phosphorus and iron. They form a very extensive group of which the different members differ considerably in physical and chemical properties, though all have certain common traits and are closely related. They are variously classified even by the latest writers. By many authors (for example Halliburton, '93) the word "*proteids*" is used in a broad sense as synonymous with *albuminous substances*, including under them the various forms of *albumin* (egg-albumin, cell-albumin, muscle-albumin, vegetable-albumins), *globulin* (fibrinogin vitellin, etc.), and the *peptones* (diffusible hydrated proteids). Another series of nearly related substances are the *albuminoids* (reckoned by some chemists among the "proteids"), examples of which are gelatin, mucin, and, according to some authors also, *nuclein*, and the *nucleo-albumins.* Some of the best authorities however, among them Kossel and Hammarsten, follow the usage of Hoppe-Seyler in restricting the word *proteid* to substances of greater complexity than the albumins and globulins. Examples of these are the nucleins and nucleo-proteids, which are compounds of nucleinic acid with albumin, histon, or protamin. The nucleo-proteids, found only in the nucleus, are not to be confounded with the nucleo-albumins, which are compounds of pseudo-nucleinic acid with albumin and yield no nuclein-bases (xanthin, hypoxanthin, adenin, guanin) as decomposition products.

---

[1] It has long been known that a form of "nuclein" may also be obtained from the nucleo-albumins of the cytoplasm, *e.g.* from the yolk of hens' eggs (vitellin). Such nucleins differ, however, from those of nuclear origin in not yielding as cleavage-products the nuclein bases (adenin, xanthin, etc.). The term "paranuclein" (Kossel) or "pseudo-nuclein" (Hammarsten) has therefore been suggested for this substance. True nucleins containing a large percentage of albumin are distinguished as *nucleo-proteids.* They may be split into albumin (or albumin radicals) and nucleinic acid, the latter yielding as cleavage-products the nuclein bases. Pseudo-nucleins containing a large percentage of albumin are designated as *nucleo-albumins*, which in like manner split into albumin and paranucleinic or pseudo-nucleinic acid, which yields no nuclein bases. (See Hammarsten, '94.)

The distribution of these substances through the cell varies greatly not only in different cells, but at different periods in the life of the same cell. The cardinal fact always, however, remains, that *there is a definite and constant contrast between nucleus and cytoplasm.* The latter always contains large quantities of nucleo-albumins, certain globulins, and sometimes small quantities of albumins and peptones; the former contains, in addition to these, *nuclein* and *nucleo-proteids,* which form its main bulk, and its most constant and characteristic feature. It is the remarkable substance, nuclein, — which is almost certainly identical with chromatin, — that chiefly claims our attention here on account of the physiological *rôle* of the nucleus.

2. *The Nuclein Series*

Nuclein was first isolated and named by Miescher, in 1871, by subjecting cells to artificial gastric digestion. The cytoplasm is thus digested, leaving only the nuclei; and in some cases, for instance pus-cells and spermatozoa, it is possible by this method to procure large quantities of nuclear substance for accurate quantitative analysis. The results of analysis show it to be a complex albuminoid substance, rich in phosphorus, for which Miescher gave the chemical formula $C_{29}H_{49}N_9P_3O_{22}$. The earlier analysis of this substance gave somewhat discordant results, as appears in the following table of percentage-compositions:[1] —

	PUS-CELLS. (HOPPE-SEYLER.)	SPERMATOZOA OF SALMON. (MIESCHER.)	HUMAN BRAIN. (V. JAKSCH.)
C	49.58	36.11	50.6
H	7.10	5.15	7.6
N	15.02	13.09	13.18
P	2.28	5.59	1.89

These differences led to the opinion, first expressed by Hoppe-Seyler, and confirmed by later investigations, that there are several varieties of nuclein which form a group having certain characters in common. Altmann ('89) opened the way to an understanding of the matter by showing that "nuclein" may be split up into two substances; namely, (1) an organic acid rich in phosphorus, to which he gave the name *nucleinic acid*, and (2) a form of albumin. Moreover, the nuclein may be synthetically formed by the re-combination of these two substances. Pure nucleinic acid, for which Miescher ('96) afterward gave the formula $C_{40}H_{54}N_{14}P_4O_{27}$,[1] contains no sulphur, a high percentage of phosphorus (above 9%), and no albumin. By adding it to a solution of albumin a precipitate is formed which contains sulphur, a lower percentage of phosphorus, and has the chemical characters of "nuclein." This indicates that the discordant results in the analyses of nuclein, referred to above, were probably due to varying proportions of the two constituents; and Altmann suggested that the "nuclein" of spermatozoa, which contains no sulphur and a maximum of phosphorus, might be uncombined nucleinic acid itself. Kossel accordingly drew the conclusion, based on his own work as well as that of Liebermann, Altmann, Malfatti, and others, that "what the histologists designate as *chromatin* consists essentially of combinations of nucleinic acid with more or less albumin, and in some cases may even be free nucleinic acid. The less the percentage of albumin in these compounds, the nearer do their properties approach those of pure nucleinic acid, and we may assume that the percentage of albumin in the chromatin of the same nucleus may vary according to physiological conditions."[2] In the same year Halliburton, following in part Hoppe-Seyler, stated the same view as follows. The so-called "nucleins" form a series leading downward from nucleinic acid thus: —

---

[1] From Halliburton, '91, p. 203. [The oxygen-percentage is omitted in this table.]

(1) Those containing no albumin and a maximum (9–10%) of phosphorus (pure nucleinic acid). Nuclei of spermatozoa.
(2) Those containing little albumin and rich in phosphorus. Chromatin of ordinary nuclei.
(3) Those with a greater proportion of albumin — a series of substances in which may probably be included *pyrenin* (nucleoli) and *plastin* (linin). These graduate into
(4) Those containing a minimum (0.5 to 1%) of phosphorus — the nucleo-albumins, which occur both in the nucleus and in the cytoplasm (vitellin, caseinogen, etc.).

Finally, we reach the globulins and albumins, especially characteristic of the cell-substance, and containing no nucleinic acid. "We thus pass by a gradual transition (from the nucleo-albumins) to the other proteid constituents of the cell, the cell-globulins, which contain no phosphorus whatever, and to the products of cell-activity, such as the proteids of serum and of egg-white, which are also principally phosphorus-free."[1] Further, "in the processes of vital activity there are changing relations between the phosphorized constituents of the nucleus, just as in all metabolic processes there is a continual interchange, some constituents being elaborated, others breaking down into simpler products." This latter conclusion has been well established; the others, as stated by Halliburton, require some modification, on the one hand, through the results of later analyses of chromatin, on the other, because of the failure to distinguish between the nucleo-proteids and the nucleo-albumins. First, it has been shown by Miescher ('96), Kossel ('96), and Mathews ('97, 2) that the chromatin of the sperm-nuclei (in fish and sea-urchins) is not pure nucleinic acid, as Altmann conjectured, but a salt of that acid, with histon, protamin, or a related substance. Thus, in the spermatozoa of the salmon, Miescher's analyses give 60.56% of nucleinic acid and 35.56% of protamin ($C_{16}H_{28}N_9O_2$). In the herring the chromatin is a compound of nucleinic acid (over 63%) and a form of protamin called by Kossel "clupein" ($C_{30}H_{57}N_{17}O_6$). In the sea-urchin *Arbacia* Mathews finds the chromatin to be a compound of nucleinic acid and "arbacin," a histon-like body. Kossel finds also that chromatin (nuclein) derived from the thymus gland, and from leucocytes, is largely a histon salt of nucleinic acid, the proportion of the latter being, however, much less than in the sperm-chromatin, while albumin is also present. In these cases, therefore, the greater part of the nucleinic acid is combined not with albumin but with a histon or protamin radical. Second, the nucleo-albumins of the cytoplasm are in no sense transitional between the nucleins and the albumins, since they contain no true nucleinic acid, but only pseudo-nucleinic acid.[2] The fact nevertheless remains that the nucleins and nucleo-proteids, though confined to the nucleus, form a series descending from such highly phosphorized bodies as the sperm-chromatin toward bodies such as the albumins, which are especially characteristic of the cytoplasm; and that they vary in composition with varying physiological conditions. The way is thus opened for a more precise investigation of the physiological *rôle* of nucleus and cytoplasm in metabolism.

---

[1] Derived from analysis of the salmon-sperm.

[2] '93, p. 158.

3. *Staining-reaction of the Nuclein Series*

In bringing these facts into relation with the staining-reactions of the cell, it is necessary briefly to consider the nature of staining-reactions in general, and especially to warn the reader that in the whole field of "micro-chemistry" we are still on such uncertain ground that all general conclusions must be taken with reserve.

First, it is still uncertain how far staining-reactions depend upon chemical reaction and how far upon merely physical properties of the bodies stained. The prevalent view that staining-reactions are due to a chemical combination of the dye with the elements of the cell has been attacked by Gierke ('85), Rawitz ('97), and Fischer ('97, '99), all of whom have endeavoured to show that these reactions are of no value as a chemical test, being only a result of surface-attraction and absorption due to purely physical qualities of the bodies stained. On the other hand, a long series of experiments, beginning with Miescher's discovery ('74) that isolated nucleinic acid forms green insoluble salts with methyl-green, and continued by Lilienfeld, Heidenhain, Paul Mayer, and others, gives strong reason to believe that beyond the physical imbibition of colour a true chemical union takes place, which, with due precautions, gives us at least a rough test of the chemical conditions existing in the cell.[1]

---

[1] '93, p. 574.

[2] *Cf.* p. 331.

Second, *similarity of staining-reaction is by no means always indicative of chemical similarity*, as is shown, for example, by the fact that in cartilage both nuclei and inter-cellular matrix are intensely stained by methyl-green, though chemically they differ very widely.

Third, colour in itself gives no evidence of chemical nature; for the nucleus and other elements of the same cell may be stained red, green, or blue, according to the dye employed, and to class them as "erythrophilous," "cyanophilous," and the like, is therefore absurd.

Fourth, *the character of the staining-reaction is influenced and in some cases determined by the fixation or other preliminary treatment*, a principle made use of practically in the operations of mordaunting, but one which may give very misleading results unless carefully controlled. Thus Rawitz ('95) shows that certain colours which ordinarily stain especially the nucleus (saffranin, gentian-violet), can be made to stain only the cytoplasm through preliminary treatment of object with solutions of tannin, followed by tartar-emetic. In like manner Mathews ('98) shows that many of the "nuclear" tar-colours (saffranin, methyl-green, etc.) stain or do not stain the cytoplasm, according as the material has been previously treated with alkaline or with acid solutions.

The results with which we now have to deal are based mainly upon experiments with tar-colours ("aniline dyes"). Ehrlich ('79) long since characterized these dyes as "acid" or "basic," according as the colouring matter plays the part of an acid or a base in the compound employed, showing further that, other things equal, the basic dyes (methyl-green, saffranin, etc.) are especially "nuclear stains" and the acid (rubin, eosin, orange, etc.) "plasma stains." Malfatti ('91), and especially Lilienfeld ('92, '93), following out Miescher's earlier work ('74), found that albumin stains preëminently in the acid stains, nucleinic acid only in the basic; and, further, that artificial nucleins, prepared by combining egg-albumin with nucleinic acid in various proportions, show a varying affinity for basic and acid dyes according as the nucleinic acid is more or less completely saturated with albumin. Lilienfeld's starting-point was given by the results of Kossel's researches on the relations of the nuclein group, which are expressed as follows:[1] —

---

[1] *Cf.* Mayer, '91, '92, '97; Lilienfeld, '93; Mathews, '98.

Nucleo-proteid (1% of P or less),
by peptic digestion splits into

Peptone | *Nuclein* (3–4% P),
by treatment with acid splits into

Albumin | *Nucleinic acid* (9–10% P),
heated with mineral acids splits into

Phosphoric acid | *Nuclein bases* (adenin, guanin, etc.). | (*A carbohydrate.*)

Now, according to Kossel and Lilienfeld, the principal nucleo-proteid in the nucleus of leucocytes is *nucleo-histon*, containing about 3% of phosphorus, which may be split into a form of *nuclein* playing the part of an acid, and an albuminoid base, the *histon* of Kossel; the nuclein may in turn be split into albumin and nucleinic acid. These four substances — albumin, nucleo-histon, nuclein, nucleinic acid — thus form a series in which the proportion of phosphorus, which is a measure of the nucleinic acid, successively increases from zero to 9–10%. If the members of this series be treated with the same mixture of red acid fuchsin and basic methyl-green, the result is as follows. Albumin (egg-albumin) is stained red, nucleo-histon greenish blue, nuclein bluish green, nucleinic acid intense green. "We see, therefore, that the principle that determines the staining of the nuclear substances is always the nucleinic acid. All the nuclear substances, from those richest in albumin to those poorest in it, or containing none, assume the tone of the nuclear (*i.e.* basic) stain, but the combined albumin modifies the green more or less toward blue."[2] Lilienfeld explains the fact that chromatin in the cell-nucleus seldom appears pure green on the assumption, supported by many facts, that the proportions of nucleinic acid and albumin vary with different physiological conditions, and he suggests further that the intense staining-power of the chromosomes during mitosis is probably due to the fact that they contain a maximum of nucleinic acid. Very interesting is a comparison of the foregoing staining-reactions with those given by a mixture of a *red basic* dye (saffranin) and a *green acid* one ("light green"). With this combination an effect is given which reverses that of the Biondi-Ehrlich mixture; *i.e.* the nuclein is coloured red, the albumin green, which is a beautiful demonstration of the fact that staining-reagents cannot be logically classified according to colour, but only according to their chemical nature, and gives additional ground for the view that staining-reactions of this type are the result of a chemical rather than a merely physical combination.

---

[1] From Lilienfeld, after Kossel ('92, p. 129).

[2] *l.c.*, p. 394.

These results must be taken with some reserve for the following reasons: Mathews ('98) has shown that methyl-green and other basic dyes will energetically stain albumose, coagulated egg-albumin, and the cell-cytoplasm in or after treatment by alkaline fluids; while conversely the acid dyes do not stain, or only slightly stain, these substances under the same conditions. This probably does not affect the validity of Heidenhain's results,[1] since he worked with acid solutions. What is more to the point is the fact that hyaline cartilage and mucin, though containing no nucleinic acid, stain intensely with basic dyes. Mathews probably gives the clue to this reaction, in the suggestion that it is here probably due to the presence of other acids (in the case of cartilage a salt of chondroitin-sulphuric acid, according to Schmiedeberg); from which Mathews concludes that the basic dyes will, in acid or neutral solutions, stain any element of the tissues that contains an organic acid in a salt combination with a strong base.[2] Accepting this conclusion, we must therefore recognize that, as far as the cytoplasm is concerned, the basic or "nuclear" stains are in no sense a test for nuclein, but only for salts of organic acids in general. In case of the nucleus, however, we know from direct analysis that we are dealing with varying combinations of nucleinic acid, and hence, with the precautions indicated above, may draw provisional conditions from the staining-reactions.

Thus regarded, the changes of staining-reaction in the chromatin are of high interest. Heidenhain ('93, '94), in his beautiful studies on leucocytes, has correlated some of the foregoing results with the staining-reactions of the cell as follows. Leucocytes stained with the Biondi-Ehrlich mixture of acid fuchsin and methyl-green show the following reactions. Cytoplasm, centrosome, attraction-sphere, astral rays, and spindle-fibres are stained pure red. The nuclear substance shows a very sharp differentiation. The chromatic network and the chromosomes of the mitotic figure are green. The linin-substance and the true nucleoli or plasmosomes appear red, like the cytoplasm. The linin-network of leucocytes is stated by Heidenhain to consist of two elements, namely, of red granules or microsomes suspended in a colourless network. The latter alone is called "linin" by Heidenhain. To the red granules is applied the term "oxychromatin," while the green substance of the ordinary chromatic network, forming the "chromatin" of Flemming, is called "basichromatin."[1] Morphologically, the granules of both kinds are exactly alike,[2] and in many cases the oxychromatin-granules are found not only in the "achromatic" nuclear network, but also intermingled with the basichromatin-granules of the chromatic network. Collating these results with those of the physiological chemists, Heidenhain concludes that basichromatin is a substance rich in phosphorus (*i.e.* nucleinic acid), oxychromatin a substance poor in phosphorus, and that, further, "basichromatin and oxychromatin are by no means to be regarded as permanent unchangeable bodies but may change their colour-reactions by combining with or giving off phosphorus." In other words, "the affinity of the chromatophilous microsomes of the nuclear network for basic and acid aniline dyes is regulated by certain physiological conditions of the nucleus or of the cell."[3]

---

[1] See below.

[2] '98, pp. 451–452.

This conclusion, which is entirely in harmony with the statements of Kossel and Halliburton quoted above, opens up the most interesting questions regarding the periodic changes in the nucleus. The staining-power of chromatin is at a maximum when in the preparatory stages of mitosis (spireme-thread, chromosomes). During the ensuing growth of the nucleus it always diminishes, suggesting that a combination with albumin has taken place. This is illustrated in a very striking way by the history of the egg-nucleus or germinal vesicle, which exhibits the nuclear changes on a large scale. It has long been known that the chromatin of this nucleus undergoes great changes during the growth of the egg, and several observers have maintained its entire disappearance at one period. Rückert first carefully traced out the history of the chromatin in detail in the eggs of sharks, and his general results have since been confirmed by Born in the eggs of *Triton*. In the shark *Pristiurus*, Rückert ('92, 1) finds that the chromosomes, which persist throughout the entire growth-period of the egg, undergo the following changes (Fig. 157): At a very early stage they are small, and stain intensely with nuclear dyes. During the growth of the egg they undergo a great increase in size, and progressively *lose their staining-capacity*. At the same time their surface is enormously increased by the development of long threads which grow out in every direction from the central axis (Fig. 157, *A*). As the egg approaches its full size, the chromosomes rapidly diminish in size, the radiating threads disappear, and the staining-capacity increases (Fig. 157, *B*). They are finally again reduced to minute, intensely staining bodies which enter into the equatorial plate of the first polar, mitotic figure (Fig. 157, *C*). How great the change of volume is may be seen from the following figures. At the beginning the chromosomes measure, at most, 12 μ (about $\frac{1}{2000}$ in.) in length and

---

[1] '94, p. 543.

[2] *l.c.*, p. 547.

[3] *l.c.*, p. 548.

$\frac{1}{2}\,\mu$ in diameter. At the height of their development they are almost eight times their original length and twenty times their original diameter. In the final period they are but $2\,\mu$ in length and $1\,\mu$ in diameter. These measurements show a change of volume so enormous, even after making due allowance for the loose structure of the large chromosomes, that it cannot be accounted for by mere swelling or shrinkage. The chromosomes evidently absorb a large amount of matter, combine with it to form a substance of diminished staining-capacity, and finally give off matter, leaving an intensely staining substance behind. As Rückert points out, the great increase of surface in the chromosomes is adapted to facilitate an exchange of material between the chromatin and the surrounding substance; and he concludes that the coincidence between the growth of the chromosomes and that of the egg points to an intimate connection between the nuclear activity and the formative energy of the cytoplasm.

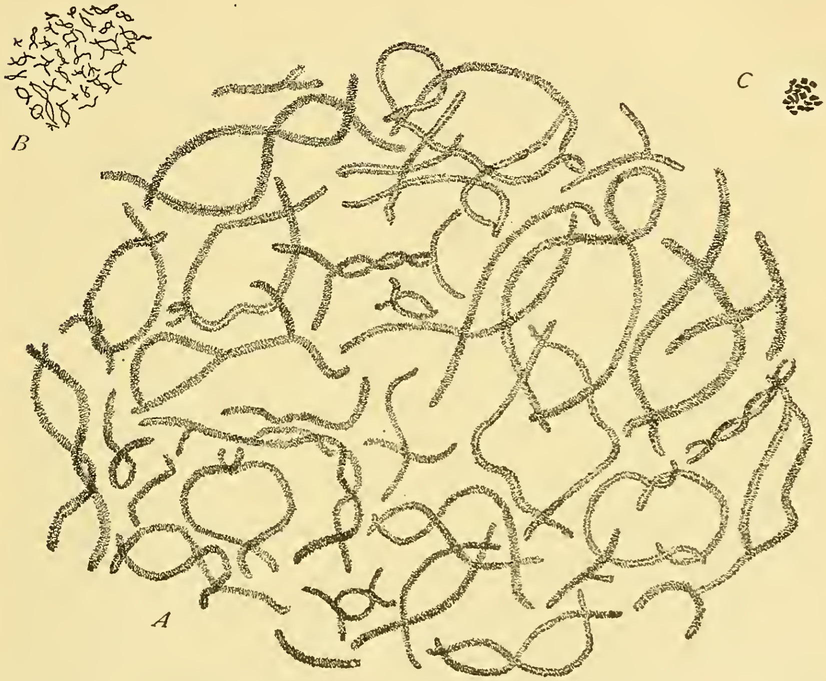

Fig. 157. — Chromosomes of the germinal vesicle in the shark *Pristiurus*, at different periods, drawn to the same scale. [RÜCKERT.]

A. At the period of maximal size and minimal staining-capacity (egg 3 mm. in diameter). *B*. Later period (egg 13 mm. in diameter). *C*. At the close of ovarian life, of minimal size and maximal staining-power.

If these facts are considered in the light of the known staining-reaction of the nuclein series, we must admit that the following conclusions are something more than mere possibilities. We may infer that the original chromosomes contain a high percentage of nucleinic acid; that their growth and loss of staining-power is due to a combination with a large amount of albuminous substance to form a lower member of the nuclein series, probably a nucleo-proteid; that their final diminution in size and resumption of staining-power is caused by a giving up of the albumin constituent, restoring the nuclein to its original state as a preparation for division. The growth and diminished staining-capacity of the chromatin occurs during a period of intense constructive activity in the cytoplasm; its diminution in bulk and resumption of staining-capacity coincides with the cessation of this activity. This result is in harmony with the observations of Schwarz and Zacharias on growing plant-cells, the percentage of nuclein in the nuclei of embryonic cells (meristem) being at first relatively large and diminishing as the cells increase in size. It agrees further with the fact that of all forms of nuclei those of the spermatozoa, in which growth is suspended, are richest in nucleinic acid, and in this respect stand at the opposite extreme from the nuclei of the rapidly growing egg-cell.

Accurately determined facts in this direction are still too scanty to admit of a safe generalization. They are, however, enough to indicate the probability that chromatin passes through a certain cycle in the life of the cell, the percentage of albumin or of albumin-radicals increasing during the vegetative activity of the nucleus, decreasing in its reproductive phase. In other words, a combination of albumin with nuclein or nucleinic acid is an accompaniment of constructive metabolism. As the cell prepares for division, the combination is dissolved and the nuclein-radicle or nucleinic acid is handed on by division to the daughter-cells. A tempting hypothesis, suggested by Mathews on the basis of Kossel's work, is that nuclein, or one of its constituent molecular groups, may in a chemical sense be regarded as the formative centre of the cell which is directly involved in the process by which food-matters are built up into the cell-substance. Could this be established, we should have not only a clear light on the changes of staining-reactions during the cycle of cell-life, but also a clue to the nuclear "control" of the cell through the process of synthetic metabolism. This hypothesis fits well with the conclusions of other physiological chemists that the nucleus is especially concerned in synthetic metabolism. Kossel concludes that the formation of new organic matter is dependent on the nucleus,[1] and that nuclein in some manner plays a leading *rôle* in this process; and he makes some interesting suggestions regarding the synthesis of complex organic matters in the living cell with nuclein as a starting-point. Chittenden, too, in a review of recent chemico-physiological discoveries regarding the cell, concludes: "The cell-nucleus may be looked upon as in some manner standing in close relation to those processes which have to do with the formation of organic substances. Whatever other functions it may possess, it evidently, through the inherent qualities of the bodies entering into its composition, has a controlling power over the metabolic processes in the cell, modifying and regulating the nutritional changes" ('94).

---

[1] Schiefferdecker and Kossel, *Gewebelehre*, p. 57.

These conclusions, in their turn, are in harmony with the hypothesis advanced twenty years ago by Claude Bernard ('78), who maintained that the cytoplasm is the seat of destructive metabolism, the nucleus the organ of constructive metabolism and organic synthesis, and insisted that the *rôle* of the nucleus in nutrition gives the key to its significance as the organ of development, regeneration, and inheritance.[1]

B. Physiological Relations of Nucleus and Cytoplasm

How nearly the foregoing facts bear on the problem of the morphological formative power of the cell is obvious; and they have in a measure anticipated certain conclusions regarding the *rôle* of nucleus and cytoplasm, which we may now examine from a somewhat different point of view.

Brücke long ago drew a clear distinction between the chemical and molecular composition of organic substances, on the one hand, and, on the other hand, their definite grouping in the cell by which arises *organization* in a morphological sense. Claude Bernard, in like manner, distinguished between *chemical synthesis*, through which organic matters are formed, and *morphological synthesis*, by which they are built into a specifically organized fabric; but he insisted that these two processes are but different phases or degrees of the same phenomenon, and that both are expressions of the nuclear activity. We have now to consider some of the evidence that the power of morphological, as well as of chemical, synthesis centres in the nucleus, and that this is therefore to be regarded as the especial organ of inheritance. This evidence is mainly derived from the comparison of nucleated and non-nucleated masses of protoplasm; from the form, position, and movements of the nucleus in actively growing or metabolizing cells; and from the history of the nucleus in mitotic cell-division, in fertilization, and in maturation.

---

[1] "Il semble donc que la cellule qui a perdu son *noyau* soit stérilisée au point de vue de la génération, c'est à dire de la synthèse morphologique, et qu'elle le soit aussi au point de vue de la synthèse chimique, car elle cesse de produire des principes immediats, et ne peut guère qu'oxyder et détruire ceux qui s'y étaient accumulés par une élaboration antérieure du noyau. Il semble donc que le *noyau* soit le *germe* de nutrition de la cellule; il attire autour de lui et élabore les matériaux nutritifs" ('78, p. 523).

1. *Experiments on Unicellular Organisms*

Brandt ('77) long since observed that enucleated fragments of *Actinosphærium* soon die, while nucleated fragments heal their wounds and continue to live. The first decisive comparison between nucleated and non-nucleated masses of protoplasm was, however, made by Moritz Nussbaum in 1884 in the case of an infusorian, *Oxytricha*. If one of these animals be cut into two pieces, the subsequent behaviour of the two fragments depends on the presence or absence of the nucleus or a nuclear fragment. The nucleated fragments quickly heal the wound, regenerate the missing portions, and thus produce a perfect animal. On the other hand, enucleated fragments, consisting of cytoplasm only, quickly perish. Nussbaum therefore drew the conclusion that the nucleus is indispensable for the formative energy of the cell. The experiment was soon after repeated by Gruber ('85) in the case of *Stentor*, another infusorian, and with the same result (Fig. 159). Fragments possessing a large fragment of the nucleus completely regenerated within twenty-four hours. If the nuclear fragment were smaller, the regeneration proceeded more slowly. If no nuclear substance were present, no regeneration took place, though the wound closed and the fragment lived for a considerable time. The only exception — but it is a very significant one — was the case of individuals in which the process of normal fission had begun; in these a non-nucleated fragment in which the formation of a new peristome had already been initiated healed the wound and completed the formation of the peri-

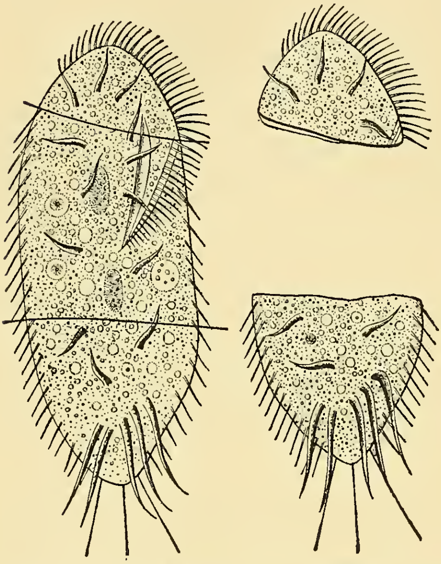

Fig. 158. — *Stylonychia*, and enucleated fragments. [VERWORN.]

At the left an entire animal, showing planes of section. The middle piece, containing two nuclei, regenerates a perfect animal. The enucleated pieces, shown at the right, swim about for a time, but finally perish.

stome. Lillie ('96) has recently found that *Stentor* may by shaking be broken into fragments of all sizes, and that nucleated fragments as small as $\frac{1}{27}$ the volume of the entire animal are still capable of complete regeneration. All non-nucleated fragments perish.

These studies of Nussbaum and Gruber formed a prelude to more extended investigations in the same direction by Gruber, Balbiani, Hofer, and especially Verworn Verworn ('88) proved that in *Polystomella*, one of the Foraminifera, nucleated fragments are able to repair the shell, while non-nucleated fragments lack this power. Balbiani ('89) showed that although non-nucleated fragments of Infusoria had no power of regeneration, they might nevertheless continue to live and swim actively about for many days after the operation, the contractile vacuole pulsating as usual. Hofer ('89), experimenting on *Amœba*, found that non-nucleated fragments might live as long as fourteen days after the operation (Fig. 160). Their movements continued, but were somewhat modified, and little by little ceased, but the pulsations of the contractile vacuole were but slightly affected; they lost more or less completely the capacity to

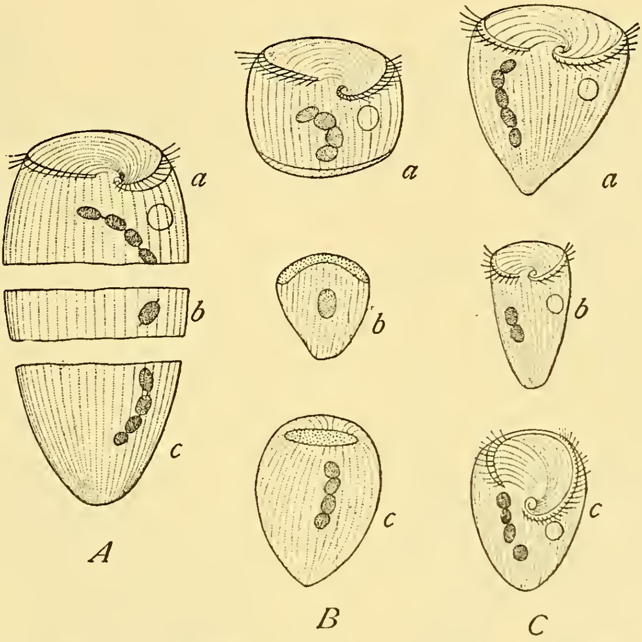

Fig. 159. — Regeneration in the unicellular animal *Stentor*. [From GRUBER after BALBIANI.]

A. Animal divided into three pieces, each containing a fragment of the nucleus. *B*. The three fragments shortly afterward. *C*. The three fragments after twenty-four hours, each regenerated to a perfect animal.

digest food, and the power of adhering to the substratum. Nearly at the same time Verworn ('89) published the results of an extended comparative investigation of various Protozoa that placed the whole matter in a very clear light. His experiments, while fully confirming the accounts of his predecessors in regard to regeneration, added many extremely important and significant results. Non-nucleated fragments both of Infusoria (*e.g. Lachrymaria*) and rhizopods (*Polystomella, Thalassicolla*) not only live for a considerable period, but perform perfectly normal and characteristic movements, show the same susceptibility to stimulus, and have the same power of ingulfing food, as the nucleated fragments. *They lack, however, the power of digestion and secretion.* Ingested food-matters may be slightly altered, but are never completely digested. The non-nucleated fragments are unable to secrete the material for a new shell (*Polysto-*

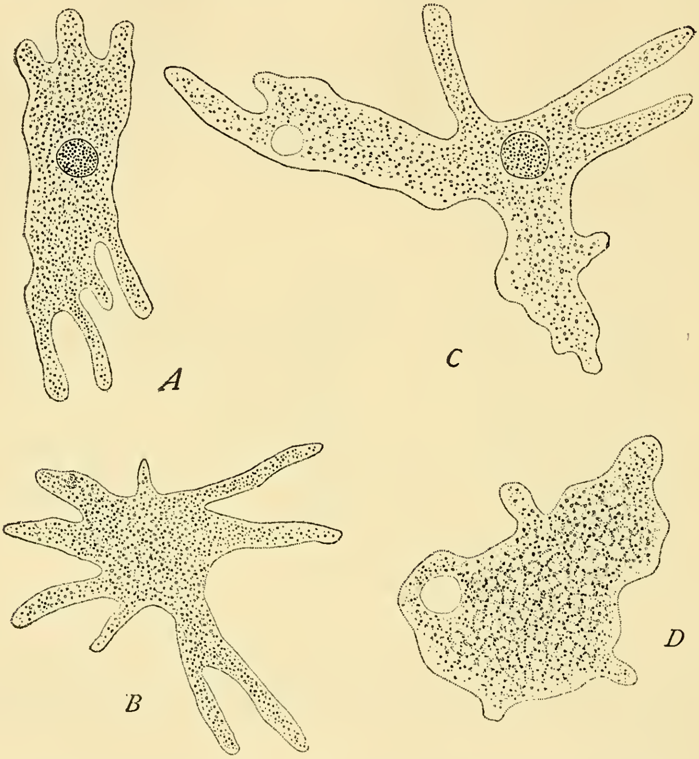

Fig. 160. — Nucleated and non-nucleated fragments of *Amœba*. [HOFER.]

A. B. An *Amœba* divided into nucleated and non-nucleated halves, five minutes after the operation. *C. D.* The two halves after eight days, each containing a contractile vacuole.

mella) or the slime by which the animals adhere to the substratum (*Amœba, Difflugia, Polystomella*). Beside these results should be placed the well-known fact that dissevered nerve-fibres in the higher animals are only regenerated from that end which remains in connection with the nerve-cell, while the remaining portion invariably degenerates.

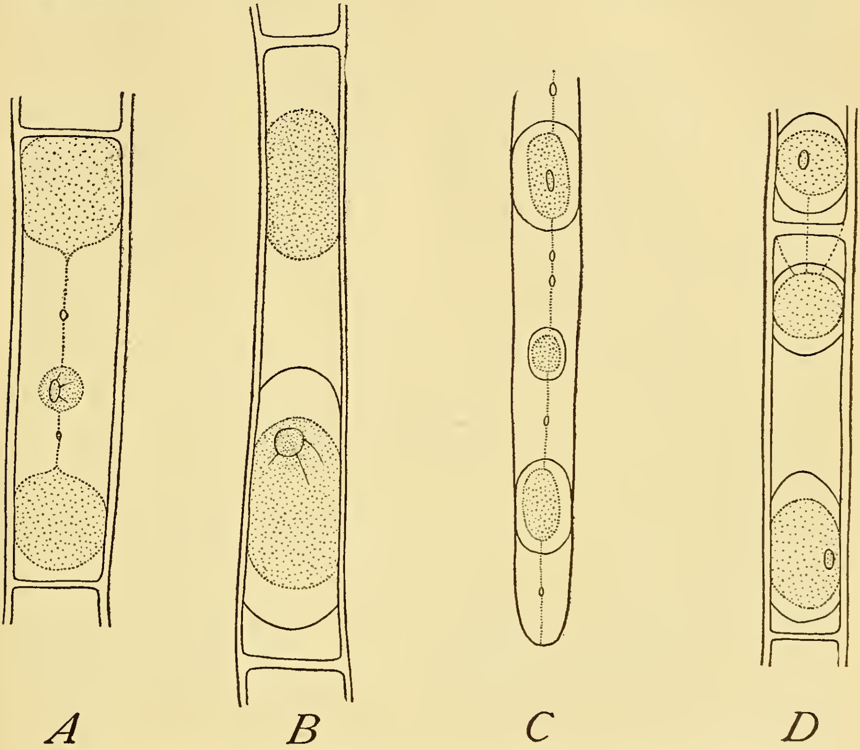

Fig. 161. — Formation of membranes by protoplasmic fragments of plasmolyzed cells. [TOWNSEND.]

A. Plasmolyzed cell, leaf-hair of *Cucurbita*, showing protoplasmic balls connected by strands. *B*. Calyx-hair of *Gaillardia;* nucleated fragment with membrane, non-nucleated one naked. *C*. Root-hair of *Marchantia;* all the fragments, connected by protoplasmic strands, have formed membranes. *D*. Leaf-hair of *Cucurbita;* non-nucleated fragment, with membrane, connected with nucleated fragment of adjoining cell.

These beautiful observations prove that destructive metabolism, as manifested by coördinated forms of protoplasmic contractility, may go on for some time undisturbed in a mass of cytoplasm deprived of a nucleus. On the other hand, the building up of new chemical or morphological products by the cytoplasm is only initiated in the presence of a nucleus and soon ceases in its absence. These facts form a complete demonstration that the nucleus plays an essential part not only in the operations of synthetic metabolism or chemical synthesis, but also in the *morphological determination of these operations, i.e.* the morphological synthesis of Bernard — a point of capital importance for the theory of inheritance, as will appear beyond.

Convincing experiments of the same character and leading to the same result have been made on the cells of plants. Francis Darwin ('77) observed more than twenty years ago that movements actively continued in protoplasmic filaments, extruded from the leaf-hairs of *Dipsacus*, that were completely severed from the body of the cell. Conversely, Klebs ('79) soon afterward showed that naked protoplasmic fragments of *Vaucheria* and other algæ were incapable of forming a new cellulose membrane if devoid of a nucleus; and he afterward showed ('87) that the same is true of *Zygnema* and *Œdogonium*. By plasmolysis the cells of these forms may be broken up into fragments, both nucleated and non-nucleated. The former surround themselves with a new wall, grow, and develop into complete plants; the latter, while able to form starch by means of the chlorophyll they contain, are incapable of utilizing it, and are devoid of the power of forming a new membrane, and of growth and regeneration. A beautiful confirmation of this is given by Townsend ('97), who finds in the case of root-hairs and pollen-tubes, that when the protoplasm is thus broken up, a membrane may be formed by both nucleated and non-nucleated fragments, by the latter however *only when they remain connected with the nucleated masses* by protoplasmic strands, however fine. If these strands be broken, the membrane-forming power is lost. Of very great interest is the further observation (made on leaf-hairs in *Cucurbita*) that the influence of the nucleus may thus extend from cell to cell, an enucleated fragment of one cell having the power to form a membrane if connected by intercellular bridges with a nucleated fragment of an adjoining cell (Fig. 161).

2. *Position and Movements of the Nucleus*

Many observers have approached the same problem from a different direction by considering the position, movements, and changes of form in the nucleus with regard to the formative activities in the cytoplasm. To review these researches in full would be impossible, and we must be content to consider only the well-known researches of Haberlandt ('77) and Korschelt ('89), both of whom have given extensive reviews of the entire subject in this regard. Haberlandt's studies related to the position of the nucleus in plant-cells with especial regard to the growth of the cellulose membrane. He determined the very significant fact that local growth of the cell-wall is always preceded by a movement of the nucleus to the point of growth. Thus, in the formation of epidermal cells, the nucleus lies at first near the centre, but as the outer wall thickens, the nucleus moves toward it, and remains closely applied to it throughout its growth, after which the nucleus often moves into another part of the cell (Fig. 162, *A*, *B*). That this is not due simply to a movement of the nucleus toward the air and light is beautifully shown in the coats of certain seeds, where the nucleus moves, not to the outer, but to the inner wall of the cell, and here the thickening takes place (Fig. 162, *C*). The same position of the nucleus is shown in the thickening of the walls of the guard-cells of stomata, in the formation of the peristome of mosses, and in many other cases. In the formation of root-hairs in the pea, the primary outgrowth always takes place from the immediate neighbourhood of the nucleus, which is carried outward and remains near the tip of the growing hair (Fig. 162, *D*, *E*). The same is true of the rhizoids of fern-prothallia and liverworts. In the hairs of aërial plants this

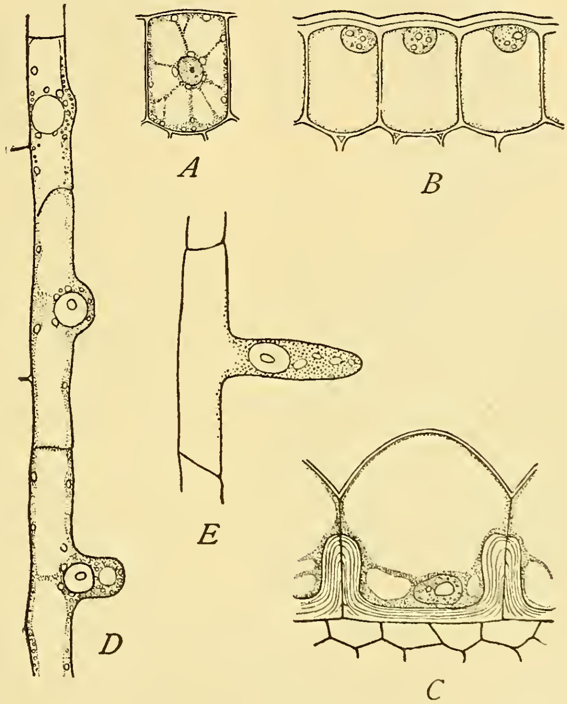

Fig. 162. — Position of the nuclei in growing plant-cells. [HABERLANDT.]

A. Young epidermal cell of *Luzula* with central nucleus, before thickening of the membrane. *B*. Three epidermal cells of *Monstera*, during the thickening of the outer wall. *C*. Cell from the seed-coat of *Scopulina*, during the thickening of the inner wall. *D*. *E*. Position of the nuclei during the formation of branches in the root-hairs of the pea.

rule is reversed, the nucleus lying near the base of the hair; but this apparent exception proves the rule, for both Hunter and Haberlandt show that in this case growth of the hair is not apical, but proceeds from the base! Very interesting is Haberlandt's observation that in the regeneration of fragments of *Vaucheria* the growing region, where a new membrane is formed, contains no chlorophyll, but numerous nuclei. The general result, based on the study of a large number of cases, is, in Haberlandt's words, that "the nucleus is in most cases placed in the neighbourhood, more or less immediate, of the points at which growth is most active and continues longest." This fact points to the conclusion that "its function is especially connected with the developmental processes of the cell,"[1] and that "in the growth of the cell, more especially in the growth of the cell-wall, the nucleus plays a definite part."

Korschelt's work deals especially with the correlation between form and position of the nucleus and the nutrition of the cell, and since it bears more directly on chemical than on morphological synthesis, may be only briefly reviewed at this point. His general conclusion is that there is a definite correlation, on the one hand, between the position of the nucleus and the source of food-supply, on the other hand, between the size of the nucleus and the extent of its surface and the elaboration of material by the cell. In support of the latter conclusion many cases are brought forward of secreting cells in which the nucleus is of enormous size and has a complex branching form. Such nuclei occur, for example, in the silk-glands of various lepidopterous larvæ (Meckel, Zaddach, etc.), which are characterized by an intense secretory activity concentrated into a very short period. Here the nucleus forms a labyrinthine network (Fig. 14, *E*), by which its surface is brought to a maximum, pointing to an active exchange of material between nucleus and cytoplasm. The same type of nucleus occurs in the Malpighian tubules of insects (Leydig, R. Hertwig), in the spinning-glands of amphipods (Mayer), and especially in the nutritive cells of the insect ovary already referred to at page 151. Here the developing ovum is accompanied and surrounded by cells, which there is good reason to believe are concerned with the elaboration of food for the egg-cell. In the earwig *Forficula* each egg is accompanied by a single large nutritive cell (Fig. 163), which has a very large nucleus rich in chromatin (Korschelt). This cell increases in size as the ovum grows, and its nucleus assumes the complex branching form shown in the figure. In the butterfly *Vanessa* there is a group of such cells at one pole of the egg, from which the latter is believed to draw its nutriment (Fig. 77). A very interesting case is that of the annelid *Ophryotrocha*, referred to at page 151. Here, as described by Korschelt, the egg floats in the perivisceral fluid, accompanied by a nurse-cell having a very large chromatic nucleus, while that of the egg is smaller and poorer in chromatin. As the egg completes its growth, the nurse-cell dwindles away and finally perishes (Fig. 76). In all these cases it is scarcely possible to doubt that the egg is in a measure relieved of the task of elaborating cytoplasmic products by the nurse-cell, and that the great development of the nucleus in the latter is correlated with this function.

---

[1] *l.c.*, p. 99.

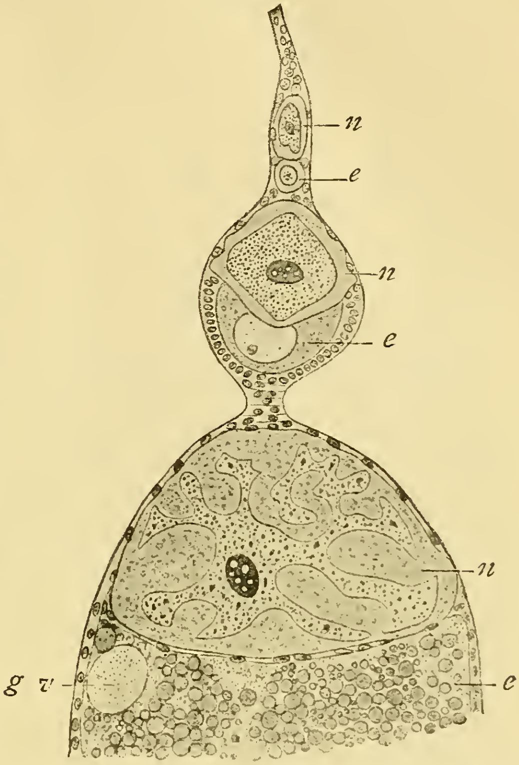

Fig. 163. — Upper portion of the ovary in the earwig *Forficula*, showing eggs and nurse-cells. [KORSCHELT.]

Below, a portion of the nearly ripe egg (*e*), showing deutoplasm-spheres and germinal vesicle (*g.v.*). Above it lies the nurse-cell (*n*) with its enormous branching nucleus. Two successively younger stages of egg and nurse are shown above.

Regarding the position and movements of the nucleus, Korschelt reviews many facts pointing toward the same conclusion. Perhaps the most suggestive of these relate to the nucleus of the egg during its ovarian history. In many of the insects, as in both the cases referred to above, the egg-nucleus at first occupies a central position, but as the egg begins to grow, it moves to the periphery on the side turned toward the nutritive cells. The same is true in the ovarian eggs of some other animals, good examples of which are afforded by various cœlenterates, *e.g.* in medusæ (Claus, Hertwig) and actinians (Korschelt, Hertwig), where the germinal vesicle is always near the point of attachment of the egg. Most suggestive of all is the case of the water-beetle *Dytiscus*, in which Korschelt was able to observe the movements and changes of form in the living object. The eggs here lie in a single series alternating with chambers of nutritive cells. The latter contain granules which are believed by Korschelt to pass into the egg, perhaps bodily, perhaps by dissolving and entering in a liquid form. At all events, the egg contains accumulations of similar granules, which extend inward in dense masses from the nutritive cells to the germinal vesicle, which they may more or less completely surround. The latter meanwhile becomes amœboid, sending out long pseudopodia, which are always directed toward the principal mass of granules (Fig. 77). The granules could not be traced into the nucleus, but the latter grows rapidly during these changes, proving that matter must be absorbed by it, probably in a liquid form.[1]

Among other facts pointing in the same direction may be mentioned Miss Hüie's ('97) observations on the gland-cells of *Drosera*, and those of Mathews ('99) on the changes of the pancreas-cell in *Necturus*. Stimulus of the gland-cells in the leaf of *Drosera* causes a rapid exhaustion and change of staining-capacity in the cytoplasm. During the ensuing repose the cytoplasm is rebuilt out of material laid down immediately around the nucleus, and agreeing closely in appearance and staining-reaction with the achromatic nuclear constituents. The chromatin increases in bulk during a period preceding the constructive phase, but decreases (while the nucleolar material increases) as the cytoplasm is restored. In the pancreas-cell, as has long been known, the "loaded" cell (before secretion) is filled with metaplasmic zymogen-granules, which disappear during secretion, the cell meanwhile becoming filled with protoplasmic fibrils (Fig. 18). During the ensuing period of "rest" the zymogen-granules are re-formed at the expense of the fibrillar material, which is finally found only at the base of the cell near the nucleus. Upon discharge of the secretion (granule-material) the fibrillæ again advance from the nucleus toward the periphery. Mathews shows that many if not all of them may be traced at one end actually into the nuclear wall, and concludes that they are directly formed by the nucleus.

Beside the foregoing facts may be placed the strong evidence reviewed at pages 156–158, indicating the formation of the yolk-nucleus, and indirectly of the yolk-material, by the nucleus. All of these and a large number of other observations in the same direction lead to the conclusion that the cell-nucleus plays an active part in nutrition, and that it is especially active during the constructive phases. On the whole, therefore, the behaviour of the nucleus in this regard is in harmony with the result reached by experiment on the one-celled forms, though it gives in itself a far less certain and convincing result.[2]

[1] Mention may conveniently here be made of Richard Hertwig's interesting observation that in starved individuals of *Actinosphærium* the chromatin condenses into a single mass, while in richly fed animals it is divided into fine granules scattered through the nucleus ('98, p. 8).

[2] Loeb ('98, '99) makes the interesting suggestion that the nucleus is especially concerned in the oxydative processes of the cell, and that this is the key to its *rôle* in the synthetic process. It has been shown that oxydations in the living tissues are probably

We now turn to evidence which, though less direct than the above, is scarcely less convincing. This evidence, which has been exhaustively discussed by Hertwig, Weismann, and Strasburger, is drawn from the history of the nucleus in mitosis, fertilization, and maturation. It calls for only a brief review here, since the facts have been fully described in earlier chapters.

3. *The Nucleus in Mitosis*

To Wilhelm Roux ('83) we owe the first clear recognition of the fact that the transformation of the chromatic substance during mitotic division is manifestly designed to effect a precise division of all its parts, — *i.e.* a panmeristic division as opposed to a mere mass-division, — and their definite distribution to the daughter-cells. "The essential operation of nuclear division is the division of the mother-granules" (*i.e.* the individual chromatin-grains); "all the other phenomena are for the purpose of transporting the daughter-granules derived from the division of a mother-granule, one to the centre of one of the daughter-cells, the other to the centre of the other." In this respect the nucleus stands in marked contrast to the cytoplasm, which undergoes on the whole a mass-division, although certain of its elements, such as the plastids and the centrosome, may separately divide, like the elements of the nucleus. From this fact Roux argued, first, that different regions of the nuclear substance must represent different qualities, and second, that the apparatus of mitosis is designed to distribute these qualities, according to a definite law, to the daughter-cells. The particular form in which Roux and Weismann developed this conception has now been generally rejected, and in any form it has some serious difficulties in its way. We cannot assume a precise localization of chromatin-elements in all parts of the nucleus; for on the one hand a large part of the chromatin may degenerate or be cast out (as in the maturation of the egg), and on the other hand in the Protozoa a small fragment of the nucleus is able to regenerate the whole. Nevertheless, the essential fact remains, as Hertwig, Kölliker, Strasburger, De Vries, and many others have insisted, that in mitotic cell-division the chromatin of the mother-cell is distributed with the most scrupulous equality to the nuclei of the daughter-cells, and that in this regard there is a most remarkable contrast between nucleus and cytoplasm. This holds true with such wonderful constancy

dependent upon certain substances (oxydation ferments) that in some manner, not yet clearly understood, facilitate the process; and the work of Spitzer ('97) has shown that these substances (obtained from tissue-extracts) belong to the group of nucleo-proteids, which are characteristic nuclear substances. The view thus suggested opens a further way toward more exact inquiry into the nuclear functions, though it is not to be supposed that the nucleus is the sole oxydative centre of the cell, as is obvious from the prolonged activity of non-nucleated protoplasmic masses.

throughout the series of living forms, from the lowest to the highest, that it must have a deep significance. And while we are not yet in a position to grasp its full meaning, this contrast points unmistakably to the conclusion that the most essential material handed on by the mother-cell to its progeny is the chromatin, and that this substance therefore has a special significance in inheritance.

4. *The Nucleus in Fertilization*

The foregoing argument receives an overwhelming reënforcement from the facts of fertilization. Although the ovum supplies nearly all the cytoplasm for the embryonic body, and the spermatozoön at most only a trace, the latter is nevertheless as potent in its effect on the offspring as the former. On the other hand, the nuclei contributed by the germ-cells, though apparently different, become in the end exactly equivalent in every visible respect — in structure, in staining-reactions, and in the number and form of the chromosomes to which each gives rise. But furthermore the substance of the two germ-nuclei is distributed with absolute equality, certainly to the first two cells of the embryo, and probably to all later-formed cells. The latter conclusion, which long remained a mere surmise, has been rendered nearly a certainty by the remarkable observations of Rückert, Zoja, and Häcker, described in Chapters IV. and VI. We must therefore accept the high probability of the conclusion that the specific character of the cell is in the last analysis determined by that of the nucleus, that is by the chromatin, and that in the equal distribution of paternal and maternal chromatin to all the cells of the offspring we find the physiological explanation of the fact that

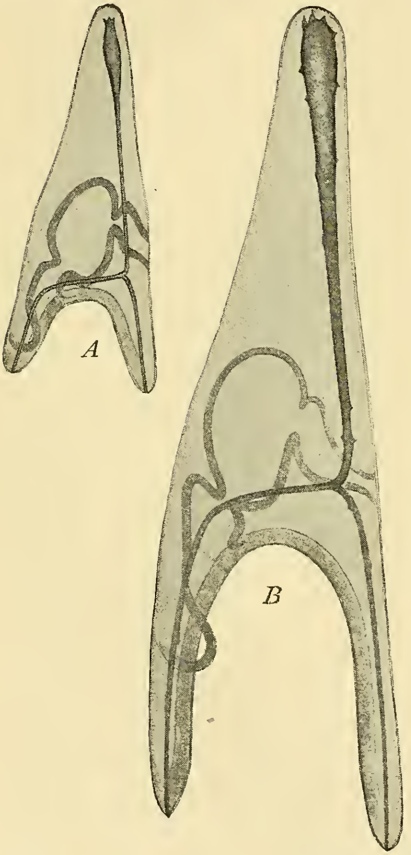

Fig. 164. — Normal and dwarf larvæ of the sea-urchin. [BOVERI.]

A. Dwarf Pluteus arising from an enucleated egg-fragment of *Sphærechinus granularis*, fertilized with spermatozoön of *Echinus microtuberculatus*, and showing *purely paternal characters*. *B.* Normal Pluteus of *Echinus microtuberculatus*.

every part of the latter may show the characteristics of either or both parents.

Boveri ('89, '95, 1) has attempted to test this conclusion by a most ingenious and beautiful experiment; and although his conclusions do not rest on absolutely certain ground, they at least open the way to a decisive test. The Hertwig brothers showed that the eggs of sea-urchins might be broken into pieces by shaking, and that spermatozoa would enter the enucleated fragments and cause them to segment. Boveri proved that such a fragment, if fertilized by a spermatozoön, would even give rise to a dwarf larva, indistinguishable from the normal in general appearance except in size. The nuclei of such larvæ are considerably smaller than those of the normal larvæ, and were shown by Morgan ('95, 4) to contain *only half the number of chromosomes*, thus demonstrating their origin from a single sperm-nucleus. Now, by fertilizing enucleated egg-fragments of one species (*Sphærechinus granularis*) with the spermatozoa of another (*Echinus microtuberculatus*), Boveri obtained in a few instances dwarf Plutei showing except in size *the pure paternal characters* (*i.e.* those of *Echinus*, Fig. 164). From this he concluded that the maternal cytoplasm has no determining effect on the offspring, but supplies only the material in which the sperm-nucleus operates. Inheritance is, therefore, effected by the nucleus alone.

The later studies of Seeliger ('94), Morgan ('95, 4), and Drisch ('98, 3) showed that this result is not entirely conclusive, since hybrid larvæ arising by the fertilization of an entire ovum of one species by a spermatozoön of the other show a very considerable range of variation; and while most such hybrids are intermediate in character between the two species, some individuals may nearly approximate to the characters of the father or the mother. Despite this fact Boveri ('95, 1) has strongly defended his conclusion, though admitting that only further research can definitely decide the question. It is to be hoped that this highly ingenious experiment may be repeated on other forms which may afford a decisive result.

5. *The Nucleus in Maturation*

Scarcely less convincing, finally, is the contrast between nucleus and cytoplasm in the maturation of the germ-cells. It is scarcely an exaggeration to say that the whole process of maturation, in its broadest sense, renders the cytoplasm of the germ-cells as unlike, the nuclei as like, as possible. The latter undergo a series of complicated changes which result in a perfect equivalence between them at the time of their union, and, more remotely, a perfect equality of distribution to the embryonic cells. The cytoplasm, on the other hand, undergoes a special differentiation in each to effect a secondary division of labour between the germ-cells. When this is correlated with the fact that the germ-cells, on the whole, have an equal effect on the specific character of the embryo, we are again forced to the conclusion that this effect must primarily be sought in the nucleus, and that the cytoplasm is in a sense only its agent.

C. The Centrosome

Existing views regarding the functions of the centrosome may conveniently be arranged in two general groups, the first including those which regard this structure as a relatively *passive* body, the second those which assume it to be an active organ. To the first belongs the hypothesis of Heidenhain ('94), accepted by Kostanecki ('97, 1) and some others, that the centrosome serves essentially as an insertion-point for the astral rays ("organic radii"), and plays a relatively passive part in the phenomena of mitosis, the active functions being mainly performed by the surrounding structures. To the same category belongs the view of Miss Foot that the formation of the centrosome is, as it were, incidental to that of the aster — "the expression, rather than the cause, of cell-activity" ('97, p. 810). To the second group belong the views of Van Beneden, Boveri, Bütschli, Carnoy, and others who regard the centrosome as playing a more active *rôle* in the life of the cell. Both of the former authors have assumed the centrosomes to be active centres by the action of which the astral systems are organized; and they are thus led to the conclusion that the centrosome is essentially an organ for cell-division and fertilization (Boveri), and in this sense is the "dynamic centre" of the cell.[1] To Carnoy and Bütschli is due the interesting suggestion[2] that the centrosomes are to be regarded further as centres of *chemical action* to which their remarkable effect on the cytoplasm is due. That the centrosome is an active centre, rather than a passive body or one created by the aster-formation, is strongly indicated by its behaviour both in mitosis and in fertilization. Griffin ('96, '99) points out that at the close of division in *Thalassema* the daughter-centrosomes migrate away from the old astral centre and incite about themselves in a different region the new astral systems for the ensuing mitosis (Figs. 99, 155); and similar conditions are described by Coe in *Cerebratulus* ('98). In fertilization the aster-formation cannot be regarded as a general action of the cytoplasm, but as a local one due to a local stimulus given by something in the spermatozoön; for in polyspermy a sperm-aster is formed for every spermatozoön (p. 198). This stimulus is given by something in the middle-piece (p. 212), which is itself genetically related to the centrosome of the last cell-generation (p. 170). These facts seem explicable only under the assumption that in these cases the centrosome, or a substance which it carries, gives an active stimulus to the cytoplasm which incites the aster-formation about itself, and in the words of Griffin "disengages the forces at work in mitosis" ('96, p. 174). For these reasons I incline to the view that in the artificial aster-formation described by Morgan[1] the centrosomes there observed should not be regarded as the creations of the asters, but rather as local deposits of material which incite the aster-formation around them. That the centrosomes or astral centres are centres of division (whether active or passive) is beautifully shown by Boveri's interesting observations on "partial fertilization" referred to at page 194.

---

[1] *Cf.* pp. 76, 192.

[2] *Cf.* p. 110.

Again, Boveri has observed that the segmenting ovum of *Ascaris* sometimes contains a supernumerary centrosome that does not enter into connection with the chromosomes, but lies alone in the cytoplasm (Fig. 165). Such a centrosome forms an independent centre of division, the cell dividing into three parts, two of which are normal blastomeres, while the third contains only the centrosome and attraction-sphere. The fate of such eggs was not determined, but they form a complete demonstration that it is in this case the centrosome and not the nucleus that determines the centres of division in the cell-body. Scarcely less conclusive is the case of dispermic eggs in sea-urchins. In such eggs both sperm-nuclei conjugate with the egg-nucleus, and both sperm-centrosomes divide (Fig. 166). The cleavage-nucleus, therefore, arises by the union of *three* nuclei and *four* centrosomes. Such eggs divide at the first cleavage into four equal blastomeres, each of which receives one of the centrosomes.

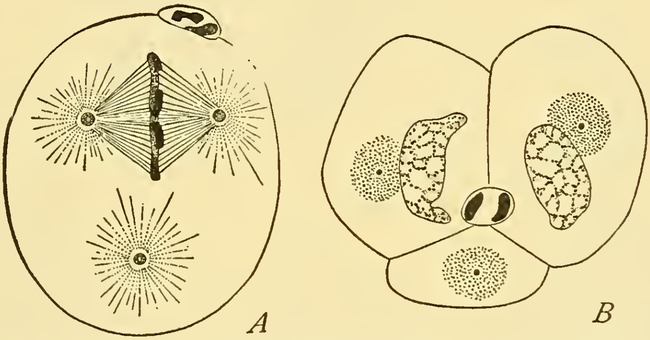

Fig. 165. — Eggs of *Ascaris* with supernumerary centrosome. [Boveri.]
A. First cleavage-spindle above, isolated centrosome below. *B.* Result of the ensuing division.

---

[1] *Cf.* p. 307.

The latter must, therefore, be the centres of division;[1] though it must not be forgotten that, in some cases at any rate, normal division requires the presence of nuclear matter (p. 108).

The centrosome must, however, be something more than a mere division-centre; for, on the one hand, in leucocytes and pigment-cells the astral system formed about it is devoted, as there is good reason to believe, not to cell-division, but to movements of the cell-body as a whole; and, on the other hand, as we have seen (pp. 165, 172), it is concerned in the formation of the flagella of the spermatozoa and spermatozoids, and probably also in that of cilia in epithelial cells. Strasburger ('97) was thus led to the conclusion that the centrosome is essentially a mass of *kinoplasm*, *i.e.* the active motor plasm,[2] and a nearly similar view has been adopted by several recent zoölogists.

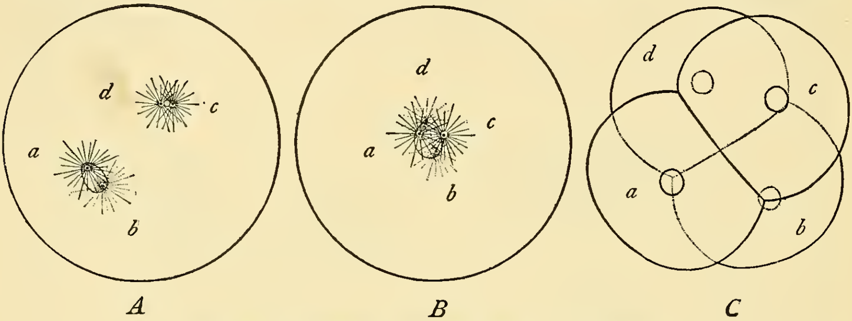

Fig. 166. — Cleavage of dispermic egg of *Toxopneustes*.

A. One sperm-nucleus has united with the egg-nucleus, shown at *a. b.*; the other lies above. Both sperm-asters have divided to form amphiasters (*a. b.* and *c. d.*). *B*. The cleavage-nucleus, formed by union of the three germ-nuclei, is surrounded by the four asters. *C*. Result of the first cleavage, the four blastomeres lettered to correspond with the four asters.

Henneguy concludes that the centrosomes are "motor centres of the kinoplasm" both for external and for internal manifestations.[3] Lenhossék regards them as "motors" for the control of ciliary action as well as for that of the spermatozoön,[4] and perhaps also for that of muscle-fibrillæ.[5] Zimmerman concludes that "the microcentrum is the motor centre of the cell, that is, the 'kinocentrum' opposed to the nucleus as the 'chemocentrum.'"[6] Regarding their control of ciliary action, he makes the same suggestion as that of Henneguy and Lenhossék cited above. He adds the further very interesting suggestions that the centrosomes may be concerned with the pseudopodial movements in the epithelial cells of the intestine, and that they may also be concerned in the protoplasmic contraction of gland-cells by which the excretion is expelled. [This is based on the fact that the centrosomes are found in the free (pseudopodia-forming) ends of the epithelial cells, and on the position of the centrosomes in goblet-cells (Fig. 23) and in those of the lachrymal gland.] Peter ('99) has attempted to test these conclusions experimentally by cutting or tearing off cilia from the cell-body (gut-epithelium of *Anodonta*) and also by isolating the tails of spermatozoa. In groups consisting of only a few cilia, separated from the nucleus, the movements actively continue, while those that are separated from the basal bodies cease to beat. Spermatozoön tails separated from the head also continue to move, but only if they remain connected with the middle-piece. Peter, therefore, supports the above conclusions of Henneguy and Lenhossék. On the other hand, Meves ('99) finds that movements of the undulating membrane in the tails of salamander-spermatozoa continue if the middle-piece be entirely removed; while a number of earlier observers[1] have observed in flagellates that a flagellum separated from the body may actively continue its movements for a considerable time.

---

[1] This phenomenon was first observed by Hertwig, and afterward by Driesch. I have repeatedly observed the internal changes in the living eggs of *Toxopneustes*.

[2] *Cf.* p. 221.

[3] '98, p. 495.

[4] '98, p. 107.

[5] '99, p. 342.

[6] '98, p. 697.

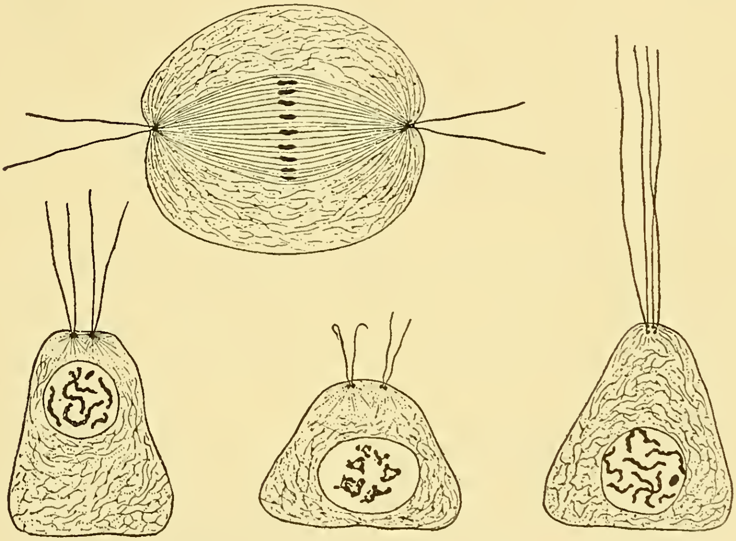

Fig. 167. — Centrosomes and cilia in spermatocytes of a butterfly. [HENNEGUY.]

Further research is therefore required to test these suggestions. The intimate connection of the centrosomes with the formation, on the one hand, of the astral rays, on the other of contractile organs, such as cilia, flagella, and pseudopodia,[1] the centrosomes in ciliated cells and spermatozoa, and in the swarm-spores of *Noctiluca*, is, however, a most striking fact, and is one of the strongest indirect arguments in favour of the general theory of fibrillar contractility in mitosis.

---

[1] See Klebs, '83, Bütschli, '85, Fischer, '94, 2.

D. Summary and Conclusion

The facts reviewed in the foregoing pages converge to the conclusion that the differentiation of the cell-substance into nucleus and cytoplasm is the expression of a fundamental physiological division of labour in the cell. Experiments upon unicellular forms demonstrate that, in the entire absence of a nucleus, protoplasm is able for a considerable time to liberate energy and to manifest coördinated activities dependent on destructive metabolism. There is here substantial ground for the view that the cytoplasm is the principal seat of these activities in the normal cell. On the other hand, there is strong cumulative evidence that the nucleus is intimately concerned in the constructive or synthetic processes, whether chemical or morphological.

That the nucleus has such a significance in synthetic metabolism is proved by the fact that digestion and absorption of food and growth soon cease with its removal from the cytoplasm, while destructive metabolism may long continue as manifested by the phenomena of irritability and contractility. It is indicated by the position and movements of the nucleus in relation to the food-supply and to the formation of specific cytoplasmic products. It harmonizes with the fact, now universally admitted, that active exchanges of material go on between nucleus and cytoplasm. The periodic changes of staining-capacity undergone by the chromatin during the cycle of cell-life, taken in connection with the researches of physiological chemists on the chemical composition and staining-reactions of the nuclein series, indicate that the phosphorus-rich substance known as *nucleinic acid* plays a leading part in the constructive process. During the vegetative phases of the cell this substance is combined with a large amount of the albumin radicles histon, protamin, and related substances, and probably in part with albumin itself, to form nuclein. During the mitotic or reproductive processes this combination appears to be dissolved, the albuminous elements being in large part split off, leaving the substance of the chromosomes with a high percentage of nucleinic acid, as is shown by direct analysis of the sperm-nucleus and is indicated by the staining-reactions of the chromosomes. There is, therefore, considerable ground for the hypothesis that in a chemical sense this substance is the most essential nuclear element handed on from cell to cell, whether by cell-division or by fertilization; and that it may be a primary factor in the constructive processes of the nucleus and through these be indirectly concerned with those of the cytoplasm.

---

[1] *Cf.* pp. 92, 102, on the central granule of the *Heliozoa.*

The *rôle* of the nucleus in constructive metabolism is intimately related with its *rôle* in morphological synthesis, and thus in inheritance; for the recurrence of similar morphological characters must in the last analysis be due to the recurrence of corresponding forms of metabolic action of which they are the outward expression. That the nucleus is in fact a primary factor in morphological as well as chemical synthesis is demonstrated by experiments on unicellular plants and animals, which prove that the power of regenerating lost parts disappears with its removal, though the enucleated fragment may continue to live and move for a considerable period. That the nuclear substance, and especially the chromatin, is a leading factor in inheritance is powerfully supported by the facts of maturation, fertilization, and cell-division. In maturation the germ-nuclei are by an elaborate process prepared for the subsequent union of equivalent chromatic elements from the two sexes. By fertilization these elements are brought together, and by mitotic division distributed with exact equality to the embryonic cells. The result, which is especially striking in the case of hybrid-fertilization, proves that the spermatozoön is as potent in inheritance as the ovum, though the latter contributes an amount of cytoplasm which is but an infinitesimal fraction of that supplied by the ovum.

It remains to be seen whether the chromatin can actually be regarded as the idioplasm or physical basis of inheritance, as maintained by Hertwig and Strasburger. Verworn has justly urged that the nucleus cannot be regarded as the sole vehicle of inheritance, since the coöperation of both nucleus and cytoplasm is essential to complete cell-life; and, as will be shown in Chapter IX., the cytoplasmic organization plays an important *rôle* in shaping the course of development. Considered in all their bearings, however, the facts seem to accord best with the hypothesis that the cytoplasmic organization is itself determined, in the last analysis, by the nucleus;[1] and the principle for which Hertwig and Strasburger contended is thus sustained.

LITERATURE. VII

Bernard, Claude. — Leçons sur les Phénomènes de la Vie: 1st ed. 1878; 2d ed. 1885. *Paris.*

Chittenden, R. H. — Some Recent Chemico-physiological Discoveries regarding the Cell: *Am. Nat.*, XXVIII., Feb., 1894.

---

[1] *Cf.* p. 431.

Fischer, A. — See Literature I.

Gruber, A. — Mikroskopische Vivisekton: *Ber. d. Naturf. Ges.* Freiburg, VII., 1893.

Haberlandt, G. — Über die Beziehungen zwischen Funktion und Lage des Zellkerns. *Fischer*, 1887.

Id. — Physiologische Pflanzenatomie. *Leipzig*, 1896.

Halliburton, W. D. — A Text-book of Chemical Physiology and Pathology. *London*, 1891.

Id. — The Chemical Physiology of the Cell (*Gouldstonian Lectures*): *Brit. Med. Journ.* 1893.

Hammarsten, O. — Lehrbuch der physiologische Chemie. 3d ed. *Wiesbaden*, 1895.

Hertwig, O. and R. — Über den Befruchtungs- und Teilungsvorgang des tierischen Eies unter dem Einfluss äusserer Agentien. *Jena*, 1887.

Kölliker, A. — Das Karyoplasma und die Vererbung, eine Kritik der Weismann'schen Theorie von der Kontinuität des Keimplasmas: *Zeitschr. wiss. Zoöl.*, XLIV. 1886.

Korschelt, E. — Beiträge sur Morphologie und Physiologie des Zellkernes: *Zoöl. Jahrb. Anat. u. Ontog.*, IV. 1889.

Kossel, A. — Über die chemische Zusammensetzung der Zelle: *Arch. Anat. u. Phys.* 1891.

Id. — Über die basischen Stoffe des Zellkernes: *Zeit. Phys. Chem.*, XXII., 1896.

Lilienfeld, L. — Über die Wahlverwandtschaft der Zellelemente zu Farbstoffen: *Arch. Anat. u. Phys.* 1893.

Malfatti, H. — Beiträge zur Kenntniss der Nucleine: *Zeitschr. Phys. Chem.*, XVI. 1891.

Mathews, A. P. — The Metabolism of the Pancreas Cell: *Journ. Morph.*, XV. *Suppl.* 1899.

Miescher, F. — Physiologisch-chemische Untersuchungen über die Lachsmilch: *Arch. Exp. Path. u. Pharm.*, XXXVII., 1896.

Prenant, A. — See Literature VI.

Rückert, J. — Zur Entwicklungsgeschichte des Ovarialeies bei Selachiern: *An. Anz.*, VII. 1892.

Sachs, J. — Vorlesungen über Pflanzen-physiologie. *Leipzig*, 1882.

Id. — Stoff und Form der Pflanzen-organe: *Gesammelte Abhandlungen*, II. 1893.

Strasburger. — See footnote, p. 269.

Verworn, M. — Die Physiologische Bedeutung des Zellkerns: *Arch. für die Ges. Phys.*, XLI. 1892.

Id. — Allgemeine Physiologie. *Jena*, 1895.

Whitman, C. O. — The Seat of Formative and Regenerative Energy: *Journ. Morph.*, II. 1888.

Zacharias, E. — Über des Verhalten des Zellkerns in wachsenden Zellen: *Flora*, 81. 1895.

CHAPTER VIII

CELL-DIVISION AND DEVELOPMENT

> "Wir können demnach endlich den Satz aufstellen, dass sämmtliche im entwickelten Zustande vorhandenen Zellen oder Aequivalente von Zellen durch eine fortschreitende Gliederung der Eizelle in morphologisch ähnliche Elemente entstehen, und dass die in einer embryonischen Organ-Anlage enthaltenden Zellen, so gering auch ihre Zahl sein mag, dennoch die ausschliessliche ungegliederte Anlage für sämmtliche Formbestandtheile der späteren Organe enthalten." REMAK.[1]

SINCE the early work of Kölliker and Remak it has been recognized that the cleavage or segmentation of the ovum, with which the development of all higher animals begins, is nothing other than a rapid series of mitotic cell-divisions by which the egg splits up into the elements of the tissues. This process is merely a continuation of that by which the germ-cell arose in the parental body. A long pause, however, intervenes during the latter period of its ovarian life, during which no divisions take place. Throughout this period the egg leads, on the whole, a somewhat passive existence, devoting itself especially to the storage of potential energy to be used during the intense activity that is to come. Its power of division remains dormant until the period of full maturity approaches. The entrance of the spermatozoön arouses in the egg a new phase of activity. Its power of division, which may have lain dormant for months or years, is suddenly raised to the highest pitch of intensity, and in a very short time it gives rise by division to a myriad of descendants which are ultimately differentiated into the elements of the tissues.

The divisions of the egg during cleavage are exactly comparable with those of tissue-cells, and all of the essential phenomena of mitosis are of the same general character in both. But for two reasons the cleavage of the egg possesses a higher interest than any other case of cell-division. First, the egg-cell gives rise by division not only to cells like itself, as is the case with most tissue-cells, but also to many other kinds of cells. The operation of cleavage is therefore immediately connected with the process of differentiation, which is the most fundamental phenomenon in development. Second, definite relations may often be traced between the planes of division and the structural axes of the adult body, and these relations are

---

[1] *Untersuchungen*, 1855, p. 140.

sometimes so clearly marked and appear so early that with the very first cleavage the position in which the embryo will finally appear in the egg may be exactly predicted. Such "promorphological" relations of the segmenting egg possess a very high interest in their bearing on the theory of germinal localization and on account of the light which they throw on the conditions of the formative process.

The present chapter is in the main a prelude to that which follows, its purpose being to sketch some of the external features of early development regarded as particular expressions of the general rules of cell-division. For this purpose we may consider the cleavage of the ovum under two heads, namely: —

1. *The Geometrical Relations of Cleavage-forms,* with reference to the general rules of cell-division.
2. *The Promorphological Relations* of the blastomeres and cleavage-planes to the parts of the adult body to which they give rise.

A. GEOMETRICAL RELATIONS OF CLEAVAGE-FORMS

The geometrical relations of the cleavage-planes and the relative size and position of the cells vary endlessly in detail, being modified by innumerable mechanical and other conditions, such as the amount and distribution of the inert yolk or deutoplasm, the shape of the ovum as a whole, and the like. Yet all the forms of cleavage can be referred to a single type which has been moulded this way or that by special conditions, and which is itself an expression of two general rules of cell-division, first formulated by Sachs in the case of plant-cells. These are: —

1. *The cell typically tends to divide into equal parts.*
2. *Each new plane of division tends to intersect the preceding plane at a right angle.*

In the simplest and least modified forms the direction of the cleavage-planes, and hence the general configuration of the cell-system, depends on the general form of the dividing mass; for, as Sachs has shown, the cleavage-planes tend to be either vertical to the surface (*anticlines*) or parallel to it (*periclines*). Ideal schemes of division may thus be constructed for various geometrical figures. In a flat circular disc, for example, the anticlinal planes pass through the radii; the periclines are circles concentric with the periphery. If the disc be elongated to form an ellipse, the periclines also become ellipses, while the anticlines are converted into hyperbolas confocal with the periclines. If it have the form of a parabola, the periclines and anticlines form two systems of confocal parabolas intersecting at right angles. All these schemes are *mutatis mutandis*, directly convertible into the corresponding solid forms in three dimensions.

Sachs has shown in the most beautiful manner that all the above ideal types are closely approximated in nature, and Rauber has applied the same principle to the cleavage of animal-cells. The discoid or spheroid form is more or less nearly realized in the thalloid growths of various lower plants, in the embryos of flowering plants, and elsewhere (Fig. 168). The paraboloid form is according to Sachs characteristic of the growing points of many higher plants; and here, too, the actual form is remarkably similar to the ideal scheme (Fig. 168, *I*).

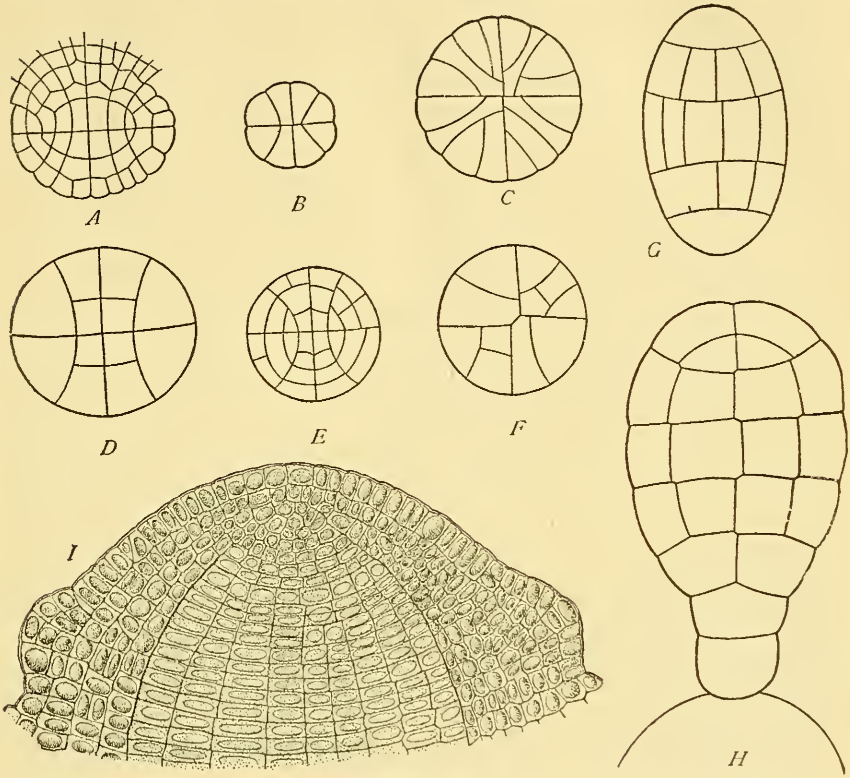

Fig. 168. — Geometrical relations of cleavage-planes in growing plant-tissues. [From SACHS, after various authors.]

A. Flat ellipsoidal germ-disc of *Melobesia* (Rosanoff); nearly typical relation of elliptic periclines and hyperbolic anticlines. *B. C.* Apical view of terminal knob on epidermal hair of *Pinguicola*. *B*. shows the ellipsoid type, *C*. the circular (spherical type), somewhat modified (only anticlines present). *D*. Growing point of *Salvinia* (Pringsheim), typical ellipsoid type; the single pericline is, however, incomplete. *E*. Growing point of *Azolla* (Strasburger); circular or spheroidal type transitional to ellipsoidal. *F*. Root-cap of *Equisetum* (Nägeli and Leitgeb); modified circular type. *G*. Cross-section of leaf-vein, *Trichomanes* (Prantl); ellipsoidal type with incomplete periclines. *H*. Embryo of *Alisma;* typical ellipsoid type, pericline incomplete only at lower side. *I*. Growing point of bud of the pine (*Abies*); typical paraboloid type, both anticlines and periclines having the form of parabolas (Sachs).

For our purpose the most important form is the sphere, which is the typical shape of the egg-cell; and all forms of cleavage may be related to the typical division of a sphere in accordance with Sachs's rules. The ideal form of cleavage would here be a succession of rectangular cleavages in the three dimensions of space, the anticlines passing through the centre so as to split the egg in the initial stages successively into halves, quadrants, and octants, the periclines being parallel to the surface so as to separate the inner ends of these cells from the outer. No case is known in which this order is accurately followed throughout, and the periclinal cleavages are of comparatively rare occurrence, being found as a regular feature of the early cleavage only in those cases where the primary germ-layers are separated by delamination. The simplest and clearest form of egg-cleavage occurs in eggs like those of echinoderms, which are of spherical form, and in which the deutoplasm is small in amount and equally distributed through its substance. Such a cleavage is beautifully displayed in the egg of the holothurian *Synapta*, as shown in the diagrams, Fig. 169, constructed from Selenka's drawings. The first cleavage is vertical, or *meridional*, passing through the egg-axis and dividing the egg into equal halves. The second, which is also meridional, cuts the first plane at right angles and divides the egg into quadrants. The third is horizontal, or *equatorial*, dividing the egg into equal octants. The order of division is thus far exactly that demanded by Sachs's rule and agrees precisely with the cleavage of various kinds of spherical plant-cells. The later cleavages depart from the ideal type in the absence of periclinal divisions, the embryo becoming hollow, and its walls consisting of a single layer of cells in which anticlinal cleavages occur in regular rectangular succession. The fourth cleavage is again meridional, giving two tiers of eight cells each; the fifth is horizontal, dividing each tier into an upper and a lower layer. The regular alternation is continued up to the ninth division (giving 512 cells), when the divisions pause while the gastrulation begins. In later stages the regularity is lost.

Hertwig's Development of Sachs's Rules. — Beside Sachs's rules may be placed two others formulated by Oscar Hertwig in 1884, which bear directly on the facts just outlined and which lie behind Sachs's principle of the rectangular intersection of successive division-planes. These are: —

1. *The nucleus tends to take up a position at the centre of its sphere of influence*, i.e. *of the protoplasmic mass in which it lies.*

2. *The axis of the mitotic figures typically lies in the longest axis of the protoplasmic mass, and division therefore tends to cut this axis at a right angle.*

The second rule explains the normal succession of the division-planes according to Sachs's second rule. The first division of a homogeneous spherical egg, for example, is followed by a second division at right angles to it, since each hemisphere is twice as long in the plane of division as in any plane vertical to it. The mitotic figure of the second division lies therefore parallel to the first plane, which forms the base of the hemisphere, and the ensuing division is vertical to it. The same applies to the third division, since each quadrant is as long as the entire egg while at most only half its diameter. Division is therefore transverse to the long axis and vertical to the first two planes.

Taken together the rules of Sachs and Hertwig, applied to the egg, give us a kind of ideal type or model, well illustrated by the cleavage of *Synapta*, described above, to which all the forms of cleavage may conveniently be referred as a basis of comparison. Numerous exceptions to all four of these rules are, however, known, and they are of little value save as a starting-point for a closer study of the facts. Cleavage of such schematic regularity as that of *Synapta* is extremely rare, both the form and the order of division being endlessly varied and in extreme cases showing scarcely a discoverable connection with the "type." We may conveniently consider these modifications under the following three heads: —

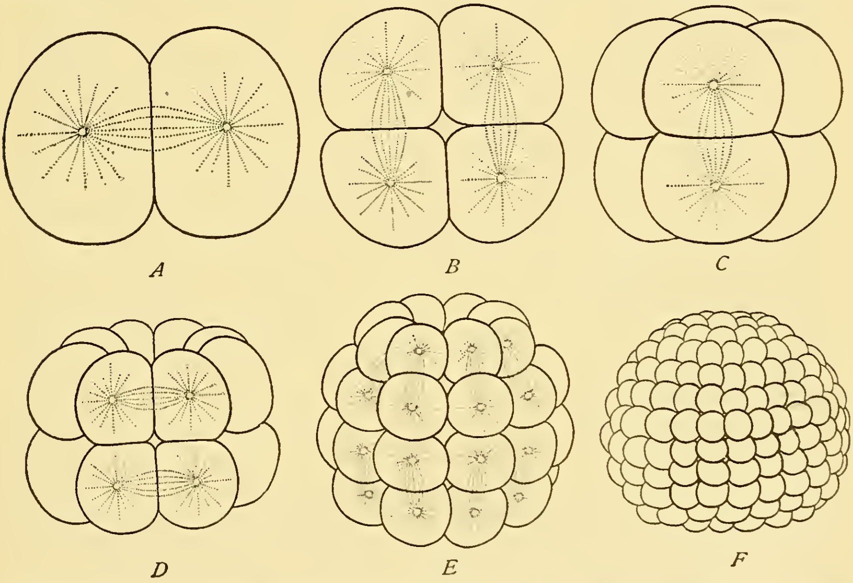

Fig. 169. — Cleavage of the ovum in the holothurian *Synapta* (slightly schematized). [After SELENKA.]

A-E. Successive cleavages to the 32-cell stage. *F.* Blastula of 128 cells.

1. *Variation in the rhythm of division.*
2. *Displacement of the cells (including variations in the direction of cleavage).*
3. *Unequal division of the cells.*

Nothing is more common than a departure from the regular rhythm of division. The variations are sometimes quite irregular, sometimes follow a definite rule, as, for instance, in the annelid *Nereis* (Fig. 171), where the typical succession in the number of cells is with great constancy 2, 4, 8, 16, 20, 23, 29, 32, 37, 38, 41, 42, after which the order is more or less variable. The factors that determine such variations in the rhythm of division are very little understood. Balfour, one of the first to consider the subject, sought an explanation in the varying distribution of metaplasmic substances, maintaining ('75, '80) that the rapidity of division in any part of the ovum is in general inversely proportional to the amount of deutoplasm that it contains. The entire inadequacy of this view has been demonstrated by a long series of precise studies on cell-lineage, which show that while the large deutoplasm-bearing cells often do divide more slowly than the smaller protoplasmic ones the reverse is often the case, while remarkable differences in the rhythm of division are often observed in cells which do not perceptibly differ in metaplasmic content.[1] All the evidence indicates that the rhythm of division is at bottom determined by factors of a very complex character which cannot be disentangled from those which control growth in general. Lillie ('95, '99) points out the very interesting fact, determined through an analysis of the cell-lineage of mollusks and annelids, that the rate of cleavage shows a direct relation to the period at which the products become functional. Thus in *Unio* the more rapid cleavage of a certain large cell ("d. 2"), formed at the fourth cleavage, is obviously correlated with the early formation of the shell-gland to which it gives rise, while the relatively slow rate of division in the first ectomere-quartet is correlated with reduction of the præ-trochal region. The prospective character shown here will be found to apply also to other characters of cleavage, as described beyond.

When we turn to the factors that determine the direction of cleavage or the displacement of cells subsequent to division, we find, as in the case of the division-rhythm, obvious mechanical factors combined with others far more complex. The arrangement of tissue-cells usually tends toward that of least resistance or greatest economy of space; and in this regard they have been shown to conform, broadly speaking, with the behaviour of elastic spheres, such as soap-bubbles when massed together and free to move. Such bodies, as Plateau and Lamarle have shown, assume a polyhedral form and tend toward such an arrangement that *the area of surface-contact between them is a minimum.* Spheres in a mass thus tend to assume the form of interlocking polyhedrons so arranged that three planes intersect in a line, while four lines and six planes meet at a point. If arranged in a single layer on an extended surface, they assume the form of hexagonal prisms, three planes meeting along a line as before. Both these forms are commonly shown in the arrangement of the cells of plant and animal tissues; and Berthold ('86) and Errera ('86, '87), carefully analyzing the phenomena, have endeavoured to show that not only the form and relative position of cells, but also the direction of cell-division, is, partially at least, thus determined.

---

[1] *Cf.* Wilson, '92, Kofoid, '94, Lillie, '95, Zur Strassen, '95, Ziegler, '95, and especially Jennings, '97.

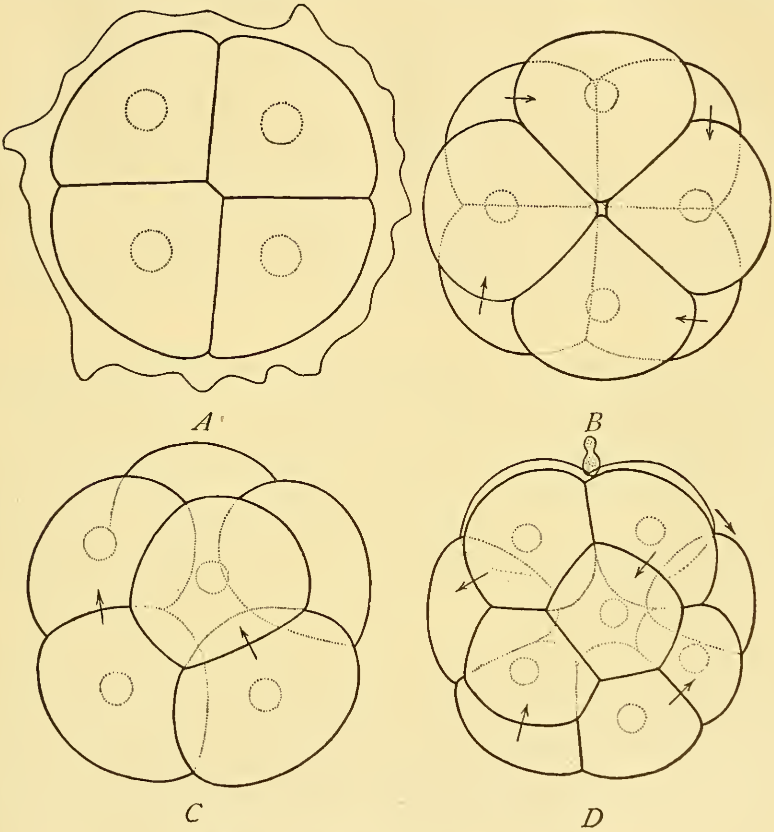

Fig. 170. — Cleavage of *Polygordius*, from life.

A. Four-cell stage, from above. *B.* Corresponding view of eight-cell stage. *C.* Side view of the same (contrast Fig. 169, *C*). *D.* Sixteen-cell stage from the side.

It is through displacements of the cells of this type that many of the most frequent modifications of cleavage arise. Sometimes, as in *Synapta*, the alternation of the cells is effected through displacement of the blastomeres after their formation. More commonly it arises during the division of the cells, and may even be predetermined by the position of the mitotic figures before the slightest external sign of division. Thus arises that form of cleavage known as the spiral, oblique, or alternating type, where the blastomeres interlock during their formation and lie in the position of least resistance from the beginning. This form of cleavage, especially characteristic of many worms and mollusks, is typically shown by the egg of *Polygordius* (Fig. 170). The four-celled stage is nearly like that of *Synapta*, though even here the cells slightly interlock. The third division is, however, oblique, the four upper cells being virtually rotated to the right (with the hands of a watch) so as to alternate with the four lower ones. The fourth cleavage is likewise oblique, but at right angles to the third, so that all of the cells interlock as shown in Fig. 170, *D*. This alternation regularly recurs for a considerable period.

In many worms and mollusks the obliquity of cleavage appears still earlier, at the second cleavage, the four cells being so arranged that two of them meet along a "cross-furrow" at the lower pole of the egg, while the other two meet at the upper pole along a similar, though often shorter, cross-furrow at right angles to the lower (*e.g.* in *Nereis*, Fig. 171). It is a curious fact that the direction of the displacement is quite constant, the first or upper quartet in the eight-cell stage being rotated to the right, or with the hands of a watch, the second quartet to the left, the third to the right, and so on. Crampton ('94) has discovered the remarkable fact that in *Physa*, a gasteropod having a reversed or sinistral shell, the whole order of displacement is likewise reversed, and the same has recently been shown by Holmes ('99) to be true of *Ancylus*.

The spiral or alternating type of cleavage beautifully illustrates Sachs's second rule as affected by modifying conditions; for, as may be seen by an inspection of Figs. 170, 171, each division-plane is approximately at right angles to the preceding and succeeding (whence the "alternation of the spirals" described by students of cell-lineage), while they are so directed that each cell as it is formed is placed at once in the position of least resistance in the mass, *i.e.* in the position of minimal surface-contact. It is impossible to resist the conclusion that one of the factors by which the position of the cells (and hence the direction of cell-division) is determined is a purely mechanical one, identical with that which determines the arrangement of soap-bubbles and the like.

Very little acquaintance with the facts of development is however required to show that this purely mechanical factor, though doubtless real, must be subordinate to some other. This is strikingly shown, for example, in the development of annelids and mollusks, where the spiral cleavage, strictly maintained during the earlier stages, finally gives way more or less completely to a bilateral type of division in which the rule of minimal surface-contact is often violated. We see here a tendency operating directly against, and finally overcoming, the mechanical factor which predominates in the earlier stages; and in some cases, *e.g.* in the egg of *Clavelina* (Fig. 177) and other tunicates, this tendency predominates from the beginning. In both these cases this "tendency" is obviously related to the growth-process to which the future bilateral embryo will owe its form;[1] and every attempt to explain the position of the cells and the direction of cleavage must reckon with the morphogenic process taken as a whole. The blastomere is not merely a cell dividing under the stress of rude

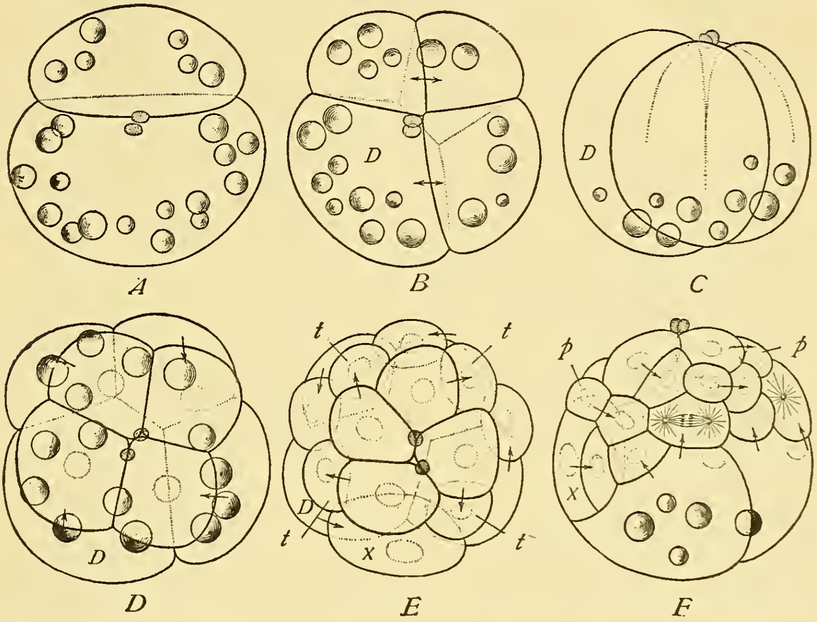

Fig. 171. — Cleavage of *Nereis*. An example of a spiral cleavage, unequal from the beginning and of a marked determinate character.

A. Two-cell stage (the circles are oil-drops). *B*. Four-cell stage; the second cleavage-plane passes through the future median plane. *C*. The same from the right side. *D*. Eight-cell stage. *E*. Sixteen cells; from the cells marked *t* arises the prototroch or larval ciliated belt, from *X* the ventral nerve-cord and other structures, from *D* the mesoblast-bands, the germ-cells, and a part of the alimentary canal. *F*. Twenty-nine-cell stage, from the right side; *p*. girdle of prototrochal cells which give rise to the ciliated belt.

---

[1] *Cf.* Wilson ('92, p. 444).

mechanical conditions; it is beyond this "a builder which lays one stone here, another there, each of which is placed with reference to future development."[1]

The third class of modifications, due to unequal division of the cells, not only leads to the most extreme types of cleavage but also to its most difficult problems. Unequal divisions appear sooner or later in all forms of cleavage, the perfect equality so long maintained in *Synapta* being a rare phenomenon. The period at which the inequality first appears varies greatly in different forms. In *Polygordius* (Fig. 170) the first marked inequality appears at the fifth cleavage;

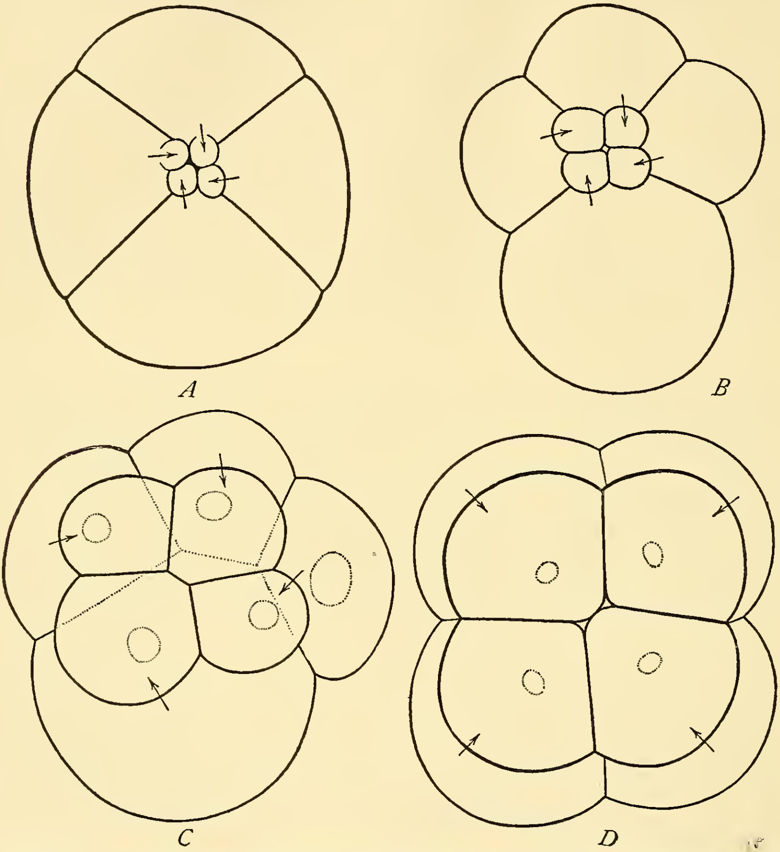

Fig. 172. — The eight-cell stage of four different animals showing gradations in the inequality of the third cleavage.

A. The leech *Clepsine* (Whitman). *B.* The chætopod *Rhynchelmis* (Vejdovský). *C.* The lamellibranch *Unio* (Lillie). *D.* *Amphioxus.*

---

[1] Lillie, '95, p. 46.

in sea-urchins it appears at the fourth (Fig. 3); in *Amphioxus* at the third (Fig. 172); in the tunicate *Clavelina* at the second (Fig. 177); in *Nereis* at the first division (Figs. 60, 171). The extent of the inequality varies in like manner. Taking the third cleavage as a type, we may trace every transition from an equal division (echinoderms, *Polygordius*), through forms in which it is but slightly marked (*Amphioxus*, frog), those in which it is conspicuous (*Nereis*, *Lymnœa*, polyclades, *Petromyzon*, etc.), to forms such as *Clepsine*, where the cells of the upper quartet are so minute as to appear like mere buds from the four large lower cells (Fig. 172). At the extreme of the series we reach the partial or meroblastic cleavage, such as occurs in the cephalopods, in many fishes, and in birds and reptiles. Here the lower hemisphere of the egg does not divide at all, or only at a late period, segmentation being confined to a disc-like region or blastoderm at one pole of the egg (Fig. 173).

Very interesting is the case of the *teloblasts* or *pole-cells* characteristic of the development of many annelids and mollusks and found in some arthropods. These remarkable cells are large blastomeres, set aside early in the development, which bud forth smaller cells in regular succession at a fixed point, thus giving rise to long cords of cells (Fig. 175). The teloblasts are especially characteristic of apical growth, such as occurs in the elongation of the body in annelids, and they are closely analogous to the apical cells situated at the growing point in many plants, such as the ferns and stoneworts.

Still more suggestive is the formation of *rudimentary cells*, arising as minute buds from the larger blastomeres, and, in some cases, apparently taking no part in the formation of the embryo (Fig. 174).[1]

We are as far removed from an explanation of unequal division as from that of the rhythm and direction of division. Inequality of division, like difference of rhythm, is often correlated with inequalities in the distribution of metaplasmic substances — a fact generalized by Balfour in the statement ('80) that the size of the cells formed in cleavage varies inversely to the relative amount of protoplasm in the region of the egg from which they arise. Thus, in all telolecithal ova, where the deutoplasm is mainly stored in the lower or vegetative hemisphere, as in many worms, mollusks, and vertebrates, the cells of the upper or protoplasmic hemisphere are smaller than those of the lower, and may be distinguished as *micromeres* from the larger *macromeres* of the lower hemisphere. The size-ratio between micromeres and macromeres is on the whole directly proportional to the ratio between protoplasm and deutoplasm. Partial or discoidal cleavage occurs when the mass of deutoplasm is so great as entirely to prevent cleavage in the lower hemisphere. This has been beautifully confirmed by O. Hertwig ('98), who, by placing frogs' eggs in a centrifugal machine, has caused them to undergo a meroblastic cleavage through the artificial accumulation of yolk at the lower pole, due to the centrifugal force.

---

[1] See Wilson, '98, '99, 2.

While doubtless containing an element of truth, this explanation is, however, no more adequate than Balfour's rule regarding the relation between deutoplasm and rhythm (p. 366); for innumerable cases are known in which no correlation can be made out between the distribution of inert substance and the inequality of division. This is the case, for example, with the teloblasts mentioned above, which contain no deutoplasm, yet regularly divide unequally. It seems to be inapplicable to the inequalities of the first two divisions in annelids and gasteropods. It is conspicuously inadequate in the history of individual blastomeres, where the history of division has been accurately determined. In *Nereis*, for example, a large cell known as the first somatoblast, formed at the fourth cleavage (*X*, Fig. 171, *E*), undergoes an invariable order of division, three unequal divisions being followed by an equal one, then by three other unequal divisions, and again by an equal. This cell contains little or no deutoplasm and undergoes no perceptible changes of substance.

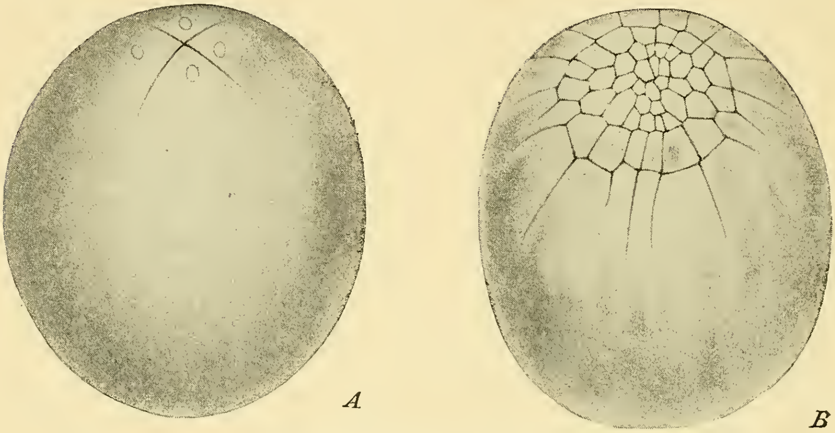

Fig. 173. — Partial or meroblastic cleavage in the squid *Loligo*. [WATASÉ.]

The collapse of the rule is most complete in case of the rudimentary cells referred to above. In some of the annelids, *e.g.* in *Aricia*, where they were first observed,[1] these cells are derived from the very large primary mesoblast-cell, which first divides into equal halves. Each of these then buds forth a cell so small as to be no larger than a polar body, and then immediately proceeds to give rise to the mesoblast-bands by continued divisions, always in the same plane at right angles to that in which the rudimentary cells are formed (Fig. 174). The cause of the definite succession of equal and unequal divisions is here wholly unexplained. No less difficult is the extreme inequality of division involved in the formation of the polar bodies. We cannot explain this through the fact that deutoplasm is collected in the lower hemisphere; for, on the one hand, the succeeding divisions (first cleavages) are often equal, while, on the other hand, the inequality is no less pronounced in eggs having equally distributed deutoplasm, or in those, like echinoderm-eggs, which are "alecithal."

---

[1] *Cf.* Wilson, '92, '98.

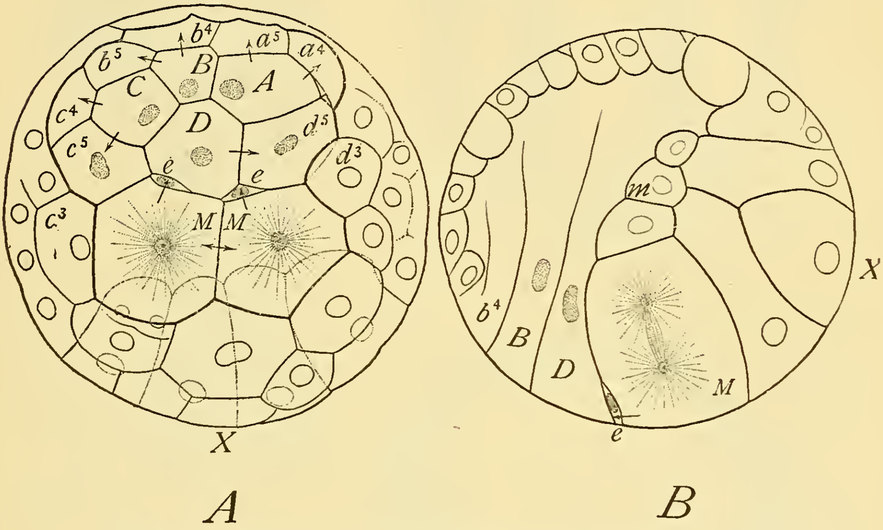

Fig. 174. — Rudimentary blastomeres in the embryo of an annelid, *Aricia*.

A. From lower pole; rudimentary cells at *e. e*; the heavy outline is the lip of the blastopore. *B*. The same in sagittal optical section, showing rudimentary cell (*e*), primary mesoblast (*M*), and mesoblast-band (*m*).

Such cases prove that Balfour's law is only a partial explanation, being probably the expression of a more deeply lying cause, and there is reason to believe that this cause lies outside the immediate mechanism of mitosis. Conklin ('94) has called attention to the fact[1] that the immediate cause of the inequality probably does not lie either in the nucleus or in the amphiaster; for not only the chromatin-halves, *but also the asters*, are exactly equal in the early prophases, and the inequality of the asters only appears as the division proceeds. Probably, therefore, the cause lies in some relation between the mitotic figure and the cell-body in which it lies.

---

[1] In the cleavage of gasteropod eggs.

I believe there is reason to accept the conclusion that this relation is one of position, however caused. A central position of the mitotic figure results in an equal division; an eccentric position caused by a radial movement of the mitotic figure, in the direction of its axis toward the periphery, leads to unequal division, and the greater the

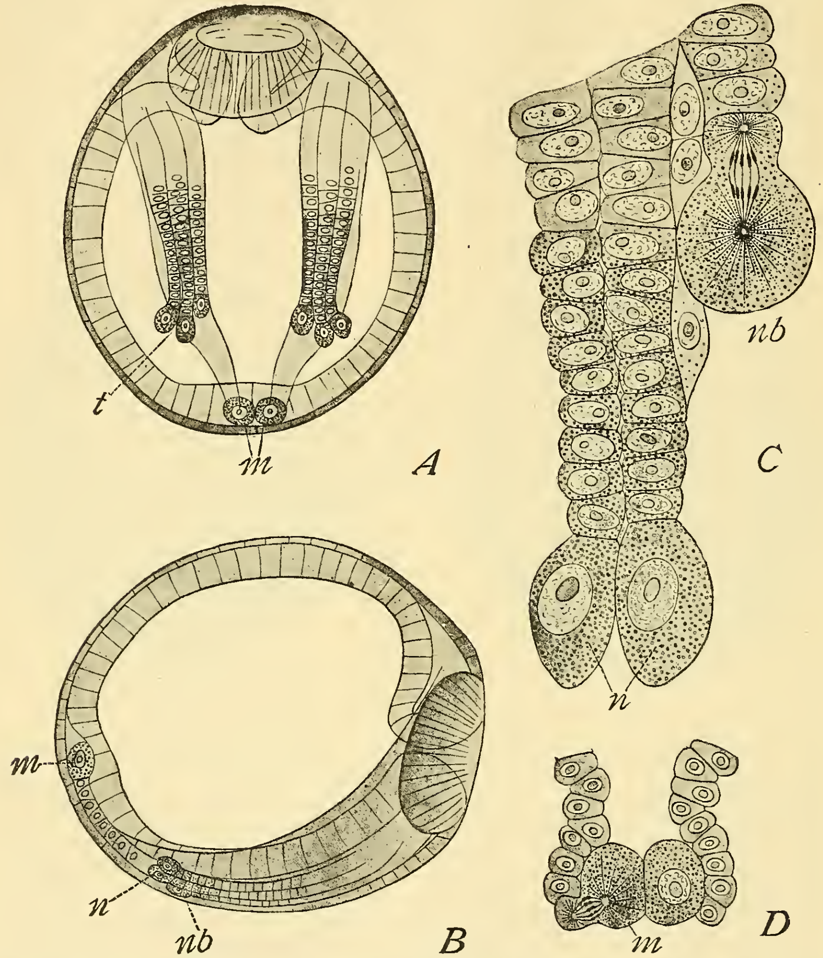

Fig. 175. — Embryos of the earthworm *Allolobophora fœtida*, showing teloblasts or apical cells. *A.* Gastrula from the ventral side. *B.* The same from the right side; *m.* the terminal teloblasts or *primary mesoblasts*, which bud forth the mesoblast-bands, cell by cell; *t.* lateral teloblasts, comprising a *neuroblast*, *nb*, from which the ventral nerve-cord arises, and two *nephroblasts*, *n*, of somewhat doubtful nature, but probably concerned in the formation of the nephridia. *C.* Lateral group of teloblasts, more enlarged, the neuroblast, *nb*, in division; *n.* the nephroblasts. *D.* The primary mesoblasts enlarged; one in division.

eccentricity, the greater the inequality, an extreme form being beautifully shown in the formation of the polar bodies. Here the original amphiaster is perfectly symmetrical, with the asters of equal size (Fig. 97, *A*). As the spindle rotates into its radial position and approaches the periphery, the development of the outer aster becomes, as it were, suppressed, while the central aster becomes enormously large. *The size of the aster, in other words, depends upon the extent of the cytoplasmic area that falls within the sphere of influence of the centrosome;* and this area depends upon the position of the centrosome. If, therefore, the polar amphiaster could be artificially prevented from moving to its peripheral position, the egg would probably divide equally.[1]

This leads us to a further consideration of the attempts that have been made to explain the movements of the mitotic figure through mechanical or other causes.[2] Highly interesting experiments have been made by Pflüger ('84), Roux ('85), Driesch ('92), and a number of later investigators which show that the direction of cleavage may be determined, or at least modified, by such a purely mechanical cause as pressure, through which the form of the dividing mass is changed.

Thus, Driesch has shown that when the eggs of sea-urchins are flattened by pressure, the amphiasters all assume the position of least resistance, *i.e.* parallel to the flattened sides, so that the cleavages are all vertical, and the egg segments as a flat plate of eight, sixteen, or thirty-two cells (Fig. 186). This is totally different from the normal form of cleavage; yet such eggs, when released from pressure, are capable of development and give rise to normal embryos. This interesting experiment makes it highly probable that the disc-like cleavage of meroblastic eggs, like that of the squid or bird, is in some degree a mechanical result of the accumulation of yolk by which the formative protoplasmic region of the ovum is reduced to a thin layer at the upper pole; and it indicates, further, that the unequal cleavage of less modified telolecithal eggs, like those of the frog or snail, are in like manner due to the displacement of the mitotic figures toward the upper pole.

The results of Pflüger's and Driesch's pressure experiments obviously harmonize with Hertwig's second rule, for the position of least resistance for the spindle is obviously in the long axis of the protoplasmic mass which is here artificially modified; and it harmonizes further with Drüner's hypothesis of the active elongation of the spindle in mitosis (p. 105). There are, however, a large number of facts which show that neither the form of the protoplasmic mass nor the distribution of metaplasmic materials is sufficient to explain the position of the spindle, whether with reference to the direction or the inequality of the cleavage.

---

[1] *Cf.* Francotte on the polar bodies of Turbellaria, p. 235.

[2] For a good review and critique, see Jennings, '97.

As regards the direction of the spindle, Berthold ('86) long since clearly pointed out that prismatic or cylindrical vegetable cells, for instance, those of the cambium, often divide lengthwise; and numerous contradictions of Hertwig's "law" have since been observed by students of cell-lineage with such accuracy that all attempts to explain them away have failed.[1] In some of these cases the position of the spindle is not that of least but of greatest resistance,[2] the spindle actually pushing away the adjoining cell to make way for itself. Similar difficulties, some of which have been already considered (p. 372), stand in the way of the attempt to explain the eccentricity of the spindle in unequal division. All these considerations drive us to the view that the simpler mechanical factors, such as pressure, form, and the like, are subordinate to far more subtle and complex operations involved in the general development of the organism, a conclusion strikingly illustrated by the phenomena of teloblastic division (p. 371), where the constant succession of unequal divisions, always in the

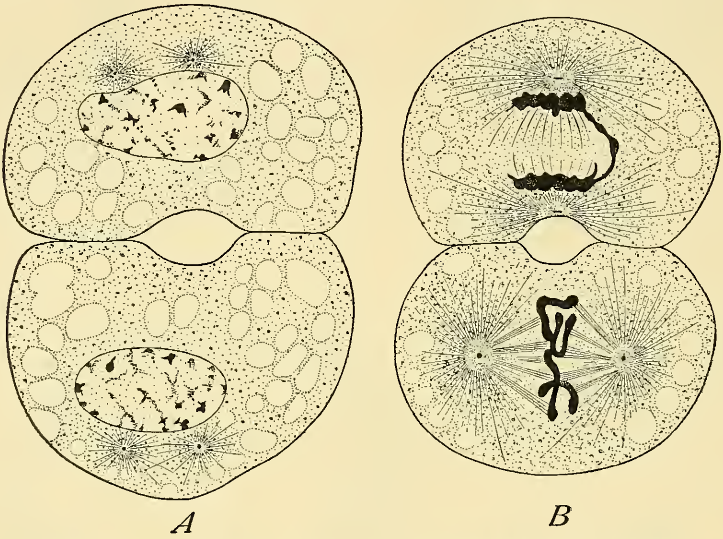

Fig. 176. — Segmenting eggs of *Ascaris*. [KOSTANECKI and SIEDLECKI.]
A. Early prophase of second division, showing double centrosomes. *B*. Second cleavage in progress; upper blastomere dividing parallel to long axis of the cell.

---

[1] *Cf.* Watasé ('91), Mead ('94, '97, 2), Heidenhain ('95), Wheeler ('95), Castle ('96), Jennings ('97).

[2] See especially the case observed by Mead ('94, '97, 2), in the egg of *Amphitrite*.

same plane, is correlated with a deeply lying law of growth affecting the entire formation of the body. *We cannot comprehend the forms of cleavage without reference to the end-result;* and thus these phenomena acquire a certain teleological character so happily expressed by Lillie (p. 370). This has been clearly recognized in various ways by a number of recent writers. Roux ('94), while seeking to explain many of the operations of mitosis on a mechanical basis, holds that the position of the spindle is partly determined by "immanent" nuclear tendencies. Braem ('94) recognizes that the position of the spindle is determined not merely as that of least resistance for the mitotic figure, but also for that of the resulting products. I pointed out ('92) that the bilateral form of cleavage in annelids must be regarded as a "forerunner" of the adult bilaterality. Jennings ('97) concludes that the form and direction of cleavage are related to the later morphogenetic processes; and many similar expressions occur in the works of recent students of cell-lineage.[1]

The clearest and best expression of this view is, however, given by Lillie ('95, '99), who not only correlates the direction and rate of cleavage, but also the size-relations of the cleavage-cells with the arrangement of the adult parts, pointing out that in general the size, as well as the position, of the blastomeres is directly correlated with that of the parts to which they give rise, and showing that on this basis "one can thus go over every detail of the cleavage, and knowing the fate of the cells, can explain all the irregularities and peculiarities exhibited."[2] Of the justice of this conclusion I think any one must be thoroughly convinced who carefully examines the recent literature of cell-lineage. It gives no real explanation of the phenomena, and is hardly more than a restatement of fact. Neither does it in any way lessen the importance of studying fully the mechanical conditions of cell-division. It does, however, show how inadequate have been most of the attempts thus far to formulate the "laws" of cell-division, and how superficially the subject has been considered by some of those who have sought for such "laws."

We now pass naturally to the second or promorphological aspect of cleavage, to a study of which we are driven by the foregoing considerations.

---

[1] Conklin ('99) believes that many of the peculiarities of cleavage may be explained by the assumption of protoplasmic currents which "carry the centrosomes where they will, and control the direction of division and the relative size and quality of the daughter-cells," *l.c.*, p. 90. He suggests that such currents are of a chemotropic character, but recognizes that their causation and direction remain unexplained.

[2] *Cf.* ('95), p. 39.

B. PROMORPHOLOGICAL RELATIONS OF CLEAVAGE

The cleavage of the ovum has thus far been considered in the main as a problem of cell-division. We have now to regard it in an even more interesting and suggestive aspect; namely, in its morphological relations to the body to which it gives rise. From what has been said above it is evident that cleavage is not merely a process by which the egg simply splits up into indifferent cells which, to use the phrase of Pflüger, have no more definite relation to the structure of the adult body than have snowflakes to the avalanche to which they contribute.[1] It is a remarkable fact that in a very large number of cases a precise relation exists between the cleavage-products and the adult parts to which they give rise; and this relation may often be traced back to the beginning of development, so that from the first division onward we are able to predict the exact future of every individual cell. In this regard the cleavage of the ovum often goes forward with a wonderful clocklike precision, giving the impression of a strictly ordered series in which every division plays a definite *rôle* and has a fixed relation to all that precedes and follows it.

But more than this, the apparent predetermination of the embryo may often be traced still farther back to the regions of the undivided and even unfertilized ovum. The egg, therefore, may exhibit a distinct promorphology; and the morphological aspect of cleavage must be considered in relation to the promorphology of the ovum of which it is an expression.

1. *Promorphology of the Ovum*

(*a*) *Polarity and the Egg-axis.* — It was long ago recognized by von Baer ('34) that the unsegmented egg of the frog has a definite *egg-axis* connecting two differentiated poles, and that the position of the embryo is definitely related to it. The great embryologist pointed out, further, that the early cleavage-planes also are definitely related to it, the first two passing through it in two meridians intersecting each other at a right angle, while the third is transverse to it, and is hence equatorial.[2] Remak afterward recognized the fact[3] that the larger cells of the lower hemisphere represent, broadly speaking, the "vegetative layer" of von Baer, *i.e.* the inner germ-layer or entoblast, from which the alimentary organs arise; while the smaller cells of the upper hemisphere represent the "animal layer," outer germ-layer or ectoblast from which arise the epidermis, the nervous system, and the sense-organs. This fact, afterward confirmed in a very large number of animals, led to the designation of the two poles as *animal* and *vegetative*, *formative* and *nutritive*, or *protoplasmic* and *deutoplasmic*, the latter terms referring to the fact that the nutritive deutoplasm is mainly stored in the lower hemisphere, and that development is therefore more active in the upper. The polarity of the ovum is accentuated by other correlated phenomena. In every case where an egg-axis can be determined by the accumulation of deutoplasm in the lower hemisphere the egg-nucleus sooner or later lies eccentrically in the upper hemisphere, and the polar bodies are formed at the upper pole. Even in cases where the deutoplasm is equally distributed or is wanting — if there really be such cases — an egg-axis is still determined by the eccentricity of the nucleus and the corresponding point at which the polar bodies are formed.

---

[1] ('83), p. 64.

[2] The third plane is in this case not precisely at the equator, but considerably above it, forming a "parallel" cleavage.

[3] '55, p. 130. Among others who early laid stress on the importance of the egg-polarity may be mentioned Auerbach ('74), Hatschek ('77), Whitman ('78), and Van Beneden ('83).

In vastly the greater number of cases the polarity of the ovum has a definite promorphological significance; for the egg-axis shows a definite and constant relation to the axes of the adult body. It is a very general rule that the upper or ectodermic pole, as marked by the position of the polar bodies, lies in the median plane at a point which is afterward found to lie at or near the anterior end. Throughout the annelids and mollusks, for example, the upper pole is the point at which the cerebral ganglia are afterward formed; and these organs lie in the adult on the dorsal side near the anterior extremity. This relation holds true for many of the Bilateralia, though the primitive relation is often disguised by asymmetrical growth in the later stages, such as occur in echinoderms. There is, however, some reason to believe that it is not a universal rule. The recent observations of Castle ('96), which are in accordance with the earlier work of Seeliger, show that in the tunicate *Ciona* the usual relation is reversed, the polar bodies being formed at the vegetative (*i.e.* deutoplasmic or entodermic) pole, which afterward becomes the dorsal side of the larva. My own observations ('95) on the echinoderm-egg indicate that here the primitive egg-axis has an entirely inconstant and casual relation to the gastrula-axis. It may, however, still be possible to show that these exceptions are only apparent, and the principle involved is too important to be accepted without further proof.

(*b*) *Axial Relations of the Primary Cleavage-planes.* — Since the egg-axis is definitely related to the embryonic axes, and since the first two cleavage-planes pass through it, we may naturally look for a definite relation between these planes and the embryonic axes; and if such a relation exists, then the first two or four blastomeres must likewise have a definite prospective value in the development. Such relations have, in fact, been accurately determined in a large number of cases. The first to call attention to such a relation seems to have been Newport ('54), who discovered the remarkable fact that *the first cleavage-plane in the frog's egg coincides with the median plane of the adult body;* that, in other words, one of the first two blastomeres gives rise to the left side of the body, the other to the right. This discovery, though long overlooked and, indeed, forgotten, was confirmed more than thirty years later by Pflüger and Roux ('87). It was placed beyond all question by a remarkable experiment by Roux ('88), who succeeded in killing one of the blastomeres by puncture with a heated needle, whereupon the uninjured cell gave rise to a half-body as if the embryo had been bisected down the middle line (Fig. 182).

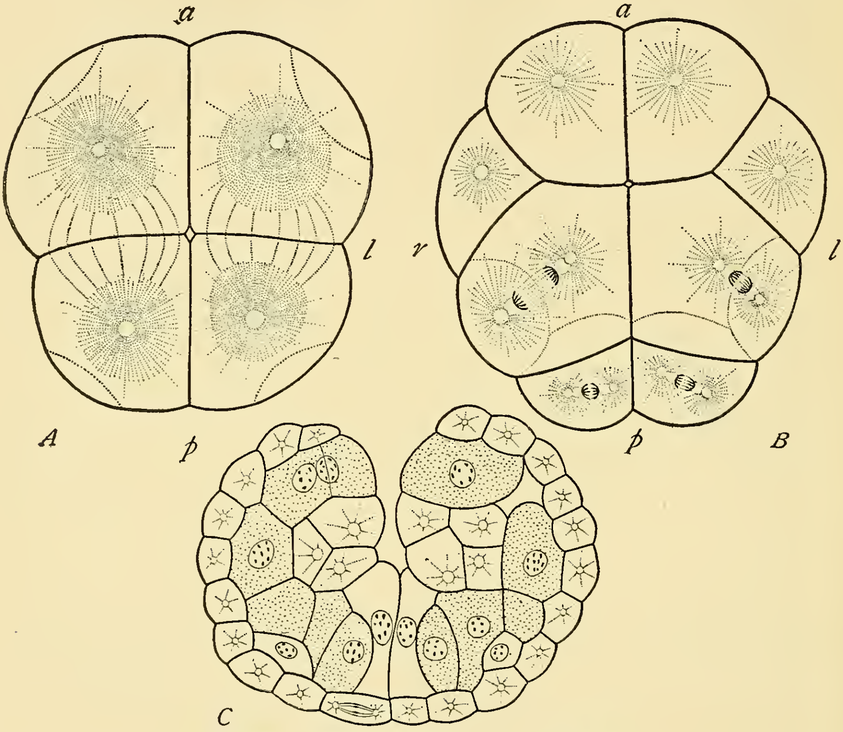

Fig. 177. — Bilateral cleavage of the tunicate egg.

A. Four-celled stage of *Clavelina*, viewed from the ventral side. *B.* Sixteen-cell stage (VAN BENEDEN and JULIN). *C.* Cross-section through the gastrula stage (CASTLE); *a.* anterior; *p.* posterior end; *l.* left, *r.* right side. [Orientation according to CASTLE.]

A similar result has been reached in a number of other animals by following out the cell-lineage; *e.g.* by Van Beneden and Julin ('84) in the egg of the tunicate *Clavelina* (Fig. 177), and by Watasé ('91) in the eggs of cephalopods (Fig. 178). In both these cases all the early stages of cleavage show a beautiful bilateral symmetry, and not only can the right and left halves of the segmenting egg be distinguished with the greatest clearness, but also the anterior and posterior regions, and the dorsal and ventral aspects. These discoveries seemed, at first, to justify the hope that a fundamental law of development had been discovered, and Van Beneden was thus led, as early as 1883, to express the view that the development of all bilateral animals would probably be found to agree with the frog and ascidian in respect to the relations of the first cleavage.

This cleavage was soon proved to have been premature. In one series of forms, not the first but the second cleavage-plane was found to coincide with the future long axis (*Nereis*, and some other annelids; *Crepidula*, *Umbrella*, and other gasteropods). In another series of forms neither of the first cleavages passes through the median plane, but both form an angle of about 45° to it (*Clepsine* and other leeches; *Rhynchelmis* and other annelids; *Planorbis*, *Nassa*, *Unio*, and other mollusks; *Discocœlis* and other platodes). In a few cases the first cleavage departs entirely from the rule, and is equatorial, as in *Ascaris* and some other nematodes. The whole subject was finally thrown into apparent confusion, first by the discovery of Clapp ('91), Jordan, and Eycleshymer ('94) that in some cases there seems to be no constant relation whatever between the early cleavage-planes and the adult axes, even in the same species (teleosts, urodeles); and even in

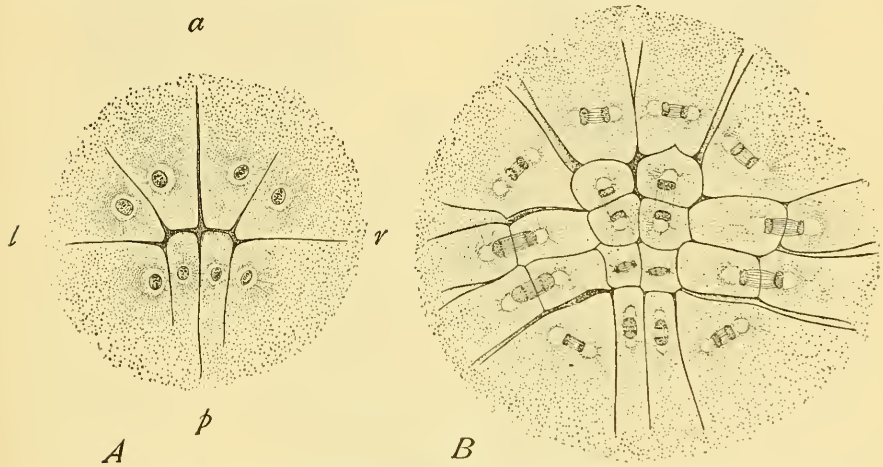

Fig. 178. — Bilateral cleavage of the squid's egg. [WATASÉ.]

A. Eight-cell stage. *B*. The fifth cleavage in progress. The first cleavage (*a-p*) coincides with the future median plane; the second (*l-r*) is transverse.

the frog Hertwig showed that the relation described by Newport and Roux is not invariable. Driesch finally demonstrated that the direction of the early cleavage-planes might be artificially modified by pressure without perceptibly affecting the end-result (*cf.* p. 375).

These facts prove that the promorphology of the early cleavage-forms can have no fundamental significance. Nevertheless, they are of the highest interest and importance; for the fact that the formative forces by which development is determined may or may not coincide with those controlling the cleavage, gives us some hope of disentangling the complicated factors of development through a comparative study of the different forms.

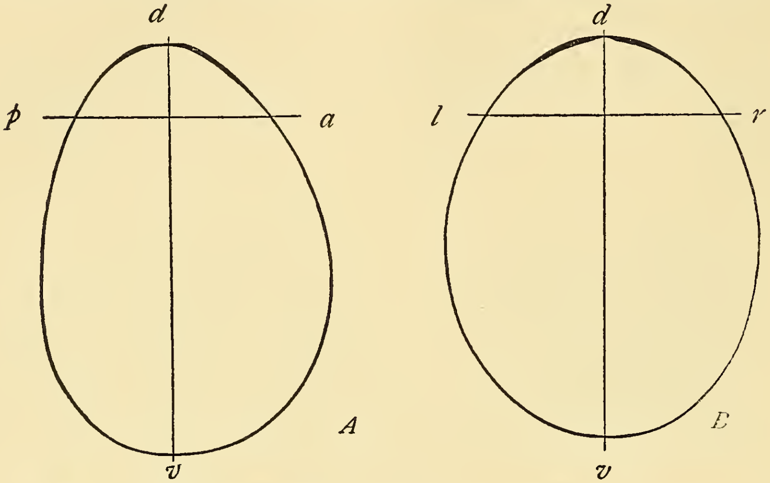

Fig. 179. — Outline of unsegmented squid's egg, to show bilaterality. [WATASÉ.]
A. From right side. *B.* From posterior aspect.
a-p. antero-posterior axis; *d-v.* dorso-ventral axis; *l.* left side; *r.* right side.

(*c*) *Other Promorphological Characters of the Ovum.* — Besides the polarity of the ovum, which is the most constant and clearly marked of its promorphological features, we are often able to discover other characters that more or less clearly foreshadow the later development. One of the most interesting and clearly marked of these is the bilateral symmetry of the ovum in bilateral animals, which is sometimes so clearly marked that the exact position of the embryo may be predicted in the unfertilized egg, sometimes even before it is laid. This is the case, for example, in the cephalopod egg, as shown by Watasé (Fig. 179). Here the form of the new-laid egg, before cleavage begins, distinctly foreshadows that of the embryonic body, and forms as it were a mould in which the whole development is cast. Its general shape is that of a hen's egg slightly flattened on one side, the narrow end, according to Watasé, representing the dorsal aspect, the broad end the ventral aspect, the flattened side the posterior region, and the more convex side the anterior region. *All the early cleavage-furrows are bilaterally arranged with respect to the plane of symmetry in the undivided egg;* and the same is true of the later development of all the bilateral parts.

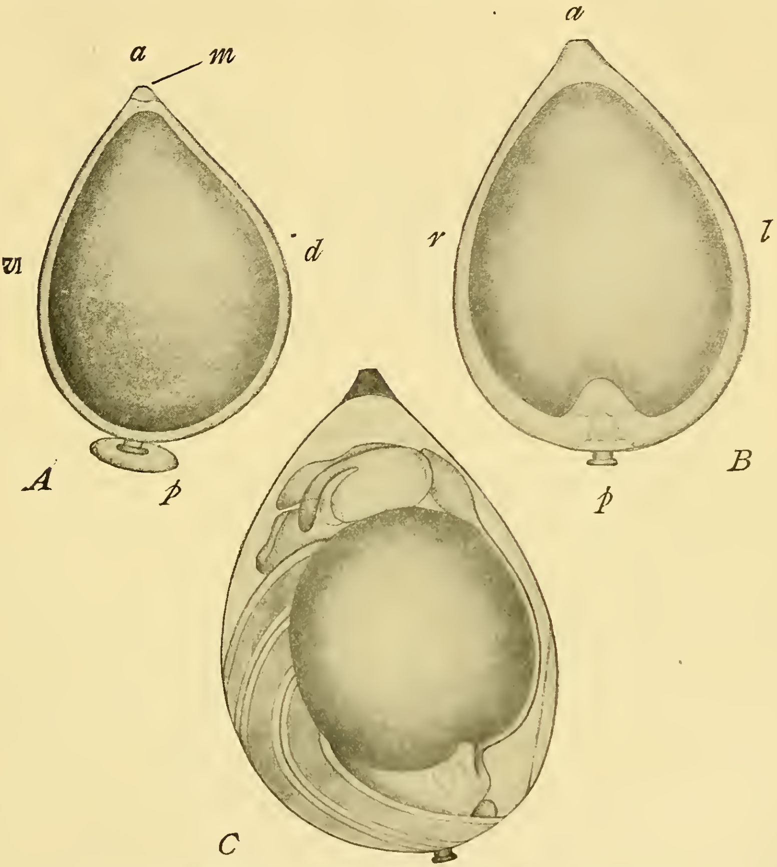

Fig. 180. — Eggs of the insect *Corixa*. [METSCHNIKOFF.]

A. Early stage before formation of the embryo, from one side. *B.* The same viewed in the plane of symmetry. *C.* The embryo in its final position.

a. anterior end; *p.* posterior; *l.* left side, *r.* right; *v.* ventral, *d.* dorsal aspect. (These letters refer to the *final* position of the embryo, which is nearly diametrically opposite to that in which it first develops); *m.* micropyle; near *p* is the pedicle by which the egg is attached.

Scarcely less striking is the case of the insect egg, as has been pointed out especially by Hallez, Blochmann, and Wheeler (Figs. 62, 180). In a large number of cases the egg is elongated and bilaterally symmetrical, and, according to Blochmann and Wheeler, may even show a bilateral distribution of the yolk corresponding with the bilaterality of the ovum. Hallez asserts as the results of a study of the cockroach (*Periplaneta*), the water-beetle (*Hydrophilus*), and the locust (*Locusta*) that "the egg-cell possesses the same orientation as the maternal organism that produces it; it has a cephalic pole and a caudal pole, a right side and a left, a dorsal aspect and a ventral; and these different aspects of the egg-cell coincide with the corresponding aspects of the embryo."[1] Wheeler ('93), after examining some thirty different species of insects, reached the same result, and concluded that even when the egg approaches the spherical form the symmetry still exists, though obscured. Moreover, according to Hallez ('86) and later writers, the egg always lies in the same position in the oviduct, its cephalic end being turned forwards toward the upper end of the oviduct, and hence toward the head-end of the mother.[2]

2. *Meaning of the Promorphology of the Ovum*

The interpretation of the promorphology of the ovum cannot be adequately treated apart from the general discussion of development given in the following chapter; nevertheless it may briefly be considered at this point. Two widely different interpretations of the facts have been given. On the one hand, it has been suggested by Flemming and Van Beneden,[3] and urged especially by Whitman,[4] that the cytoplasm of the ovum possesses a definite primordial organization which exists from the beginning of its existence even though invisible, and is revealed to observation through polar differentiation, bilateral symmetry, and other obvious characters in the unsegmented egg. On the other hand, it has been maintained by Pflüger, Mark, Oscar Hertwig, Driesch, Watasé, and the writer that all the promorphological features of the ovum are of secondary origin; that the egg-cytoplasm is at the beginning isotropous — *i.e.* indifferent or homaxial — and gradually acquires its promorphological features during its preëmbryonic history. Thus the egg of a bilateral animal is at the beginning not actually, but only potentially, bilateral. Bilaterality once established, however, it forms as it were the mould in which the cleavage and other operations of development are cast.

I believe that the evidence at our command weighs heavily on the side of the second view, and that the first hypothesis fails to take sufficient account of the fact that development does not necessarily begin with fertilization or cleavage, but may begin at a far earlier period during ovarian life. As far as the *visible* promorphological features of the ovum are concerned, this conclusion is beyond question. The only question that has any meaning is whether these visible characters are merely the expression of a more subtle preëxisting invisible organization of the same kind. I do not believe that this question can be answered in the affirmative save by the trite and, from this point of view, barren statement that every effect must have its preëxisting cause. That the egg possesses no fixed and predetermined cytoplasmic localization with reference to the adult parts, has, I think, been demonstrated through the remarkable

---

[1] See Wheeler, '93, p. 67.

[2] The micropyle usually lies at or near the anterior end, but may be at the posterior. It is a very important fact that the position of the polar bodies varies, being sometimes at the anterior end, sometimes on the side, either dorsal or lateral (Heider, Blochmann).

[3] See p. 298.

[4] *Cf.* pp. 299, 300.

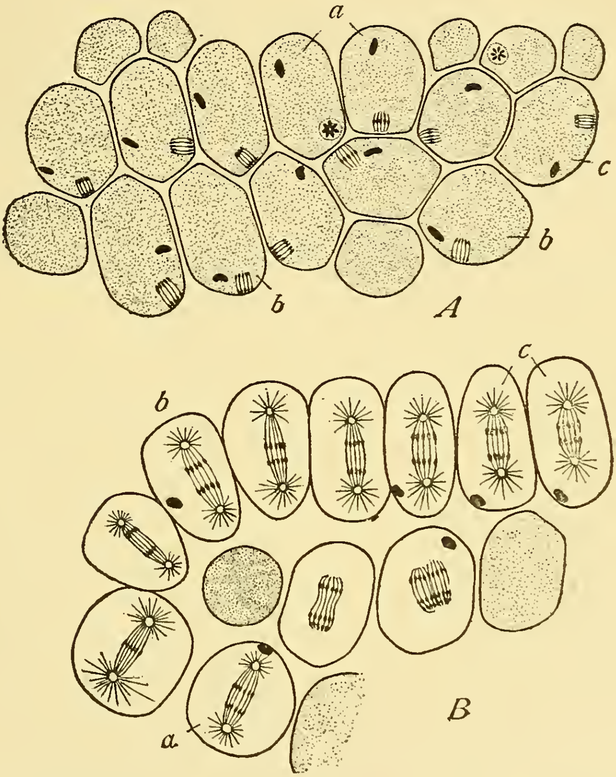

Fig. 181. — Variations in the axial relations of the eggs of *Cyclops*. From sections of the eggs as they lie in the oviduct. [HÄCKER.]

A. Group of eggs showing variations in relative position of the polar spindles and the sperm-nucleus (the latter black); in *a* the sperm-nucleus is opposite to the polar spindle, in *b*, near it or at the side. *B*. Group showing variations in the axis of first cleavage with reference to the polar bodies (the latter black); *a*, *b*, and *c* show three different positions.

experiments of Driesch, Roux, and Boveri, which show that a fragment of the egg may give rise to a complete larva (p. 353). There is strong evidence, moreover, that the egg-axis is not primordial but is established at a particular period; and even after its establishment it may be entirely altered by new conditions. This is proved, for example, by the case of the frog's egg, in which, as Pflüger ('84), Born ('85), and Schultze ('94) have shown, the cytoplasmic materials may be entirely rearranged under the influence of gravity, and a new axis established. In sea-urchins, my own observations ('95) render it probable that the egg-axis is not finally established until after fertilization. These and other facts, to be more fully considered in the following chapter, give strong ground for the conclusion that the promorphological features of the egg are as truly a result of development as the characters coming into view at later stages. They are gradually established during the preëmbryonic stages, and the egg, when ready for fertilization, has already accomplished part of its task by laying the basis for what is to come.

Mark, who was one of the first to examine this subject carefully, concluded that the ovum is at first an indifferent or homaxial cell (*i.e.* isotropic), which afterward *acquires* polarity and other promorphological features.[1] The same view was very precisely formulated by Watasé in 1891, in the following statement, which I believe to express accurately the truth: "It appears to me admissible to say at present that the ovum, which may start out without any definite axis at first, may acquire it later, and at the moment ready for its cleavage the distribution of its protoplasmic substances may be such as to exhibit a perfect symmetry, and the furrows of cleavage may have a certain definite relation to the inherent arrangement of the protoplasmic substances which constitute the ovum. Hence, in a certain case, the plane of the first cleavage-furrow may coincide with the plane of the median axis of the embryo, and the sundering of the protoplasmic material may take place into right and left, according to the preëxisting organization of the egg at the time of cleavage; and in another case the first cleavage may roughly correspond to the differentiation of the ectoderm and the entoderm, also according to the preorganized constitution of the protoplasmic materials of the ovum.

"It does not appear strange, therefore, that we may detect a certain structural differentiation in the unsegmented ovum, with all the axes foreshadowed in it, and the axial symmetry of the embryonic organism identical with that of the adult."[2]

This passage contains, I believe, the gist of the whole matter, as far as the promorphological relations of the ovum and of cleavage-forms are concerned, though Watasé does not enter into the question as to how the arrangement of protoplasmic materials is effected. In considering this question, we must hold fast to the fundamental fact that the egg is a cell, like other cells, and that from an *a priori* point of view there is every reason to believe that the cytoplasmic differentiations that it undergoes must arise in essentially the same way as in other cells. We know that such differentiations, whether in form or in internal structure, show a definite relation to the environment of the cell — to its fellows, to the source of food, and the like. We know further, as Korschelt especially has pointed out, that *the egg-axis, as expressed by the eccentricity of the germinal vesicle, often shows a definite relation to the ovarian tissues*, the germinal vesicle lying near the point of attachment or of food-supply. Mark made the pregnant suggestion, in 1881, that the primary polarity of the egg might be determined by "*the topographical relation of the egg* (when still in an indifferent state) *to the remaining cells of the maternal tissue from which it is differentiated*," and added that this relation might operate through the nutrition of the ovum. "It would certainly be interesting to know if that phase of polar differentiation which is manifest in the position of the nutritive substance and of the germinal vesicle bears a constant relation to the free surface of the epithelium from which the egg takes its origin. If, in cases where the egg is directly developed from epithelial cells, this relationship were demonstrable, it would be fair to infer the existence of corresponding, though obscured, relations in those cases where (as, for example, in mammals) the origin of the ovum is less directly traceable to an epithelial surface."[1] The polarity of the egg would therefore be comparable to the polarity of epithelial or gland-cells, where, as pointed out at page 57, the nucleus usually lies toward the base of the cell, near the source of food, while the centrosomes, and often also characteristic cytoplasmic products, such as zymogen granules and other secretions, appear in the outer portion.[2] The exact conditions under which the ovarian egg develops are still too little known to allow of a positive conclusion regarding Mark's suggestion. Moreover, the force of Korschelt's observation is weakened by the fact that in many eggs of the extreme telolecithal type, where the polarity is very marked, the germinal vesicle occupies a central or sub-central position during the period of yolk-formation and only moves toward the periphery near the time of maturation.

---

[1] '81, p. 512.

[2] '91, p. 280.

Indeed, in mollusks, annelids, and many other cases, the germinal vesicle remains in a central position, surrounded by yolk on all sides, until the spermatozoön enters. Only then does the egg-nucleus move to the periphery, the deutoplasm become massed at one pole, and the polarity of the egg come into view (*Nereis*, Figs. 60 and 97).[1] In such cases the axis of the egg may perhaps be predetermined by the position of the centrosome, and we have still to seek the causes by which the position is established in the ovarian history of the egg. These considerations show that this problem is a complex one, involving, as it does, the whole question of cell-polarity; and I know of no more promising field of investigation than the ovarian history of the ovum with reference to this question. That Mark's view is correct in principle is indicated by a great array of general evidence considered in the following chapter, where its bearing on the general theory of development is more fully dealt with.

---

[1] '81, p. 515.

[2] Hatschek has suggested the same comparison (*Zoölogie*, p. 112).

C. Cell-division and Growth

The general relations between cell-division and growth, which have already been briefly considered at page 58 and in the course of this chapter, may now be more critically examined, together with some account of the causes that incite or inhibit division. It has been shown above that every precise inquiry into the rate form, or direction of cell-division, inevitably merges into the larger problem of the general determination of growth. We may conveniently approach this subject by considering first the energy of division and the limitation of growth.

All animals and plants have a limit of growth, which is, however, much more definite in some forms than in others, and differs in different tissues. During the individual development the energy of cell-division is most intense in the early stages (cleavage) and diminishes more and more as the limit of growth is approached. When the limit is attained a more or less definite equilibrium is established, some of the cells ceasing to divide and perhaps losing this power altogether (nerve-cells), others dividing only under special conditions (connective tissue-cells, gland-cells, muscle-cells), while others continue to divide throughout life, and thus replace the worn-out cells of the same tissue (Malpighian layer of the epidermis, etc.). The limit of size at which this state of equilibrium is attained is an hereditary character, which in many cases shows an obvious relation to the environment, and has therefore probably been determined and is maintained by natural selection. From the cytological point of view the limit of body-size appears to be correlated with the total *number* of cells formed rather than with their individual size. This relation has been carefully studied by Conklin ('96) in the case of the gasteropod *Crepidula*, an animal which varies greatly in size in the mature condition, the dwarfs having in some cases not more than $\frac{1}{25}$ the volume of the giants. The eggs are, however, of the same size in all, and their *number* is proportional to the size of the adult. The same is true of the tissue-cells. Measurements of cells from the epidermis, the kidney, the liver, the alimentary epithelium, and other tissues show that they are on the whole as large in the dwarfs as in the giants. The body-size therefore depends on the total number of cells rather than on their size individually considered, and the same appears to be the case in plants.[1]

---

[1] The immature egg of *Nereis* shows, however, a distinct polarity in the arrangement of the fat-drops, which form a ring in the equatorial regions.

A result which, broadly speaking, agrees with the foregoing, is given through the interesting experimental studies of Morgan ('95, 1, '96), supplemented by those of Driesch ('98), in which the number of cells in normal larvæ of echinoderms, ascidians, and *Amphioxus* is compared with those in dwarf larvæ of the same species developed from egg-fragments (Morgan) and isolated blastomeres (Driesch). Unless otherwise specified, the following data are cited from Driesch.

The normal blastula of *Sphærechinus* possesses about 500 cells (Morgan), of which from 75 to 90 invaginate to form the archenteron (Driesch). In half-gastrulas the number varies from 35 to 45, occasionally reaching 50. In the same species, the normal number of mesenchyme-cells is 54 to 60, in the half-larvæ 25 to 30. In *Echinus* the corresponding numbers are 30± and 13 to 15. In the ascidian larvæ — a particularly favourable object — there are 29 to 35 (exceptionally as high as 40) chorda-cells; in the half-larvæ, 13 to 17. While these comparisons are not mathematically precise, owing to the difficulty of selecting exactly equivalent stages, they nevertheless show that, on the whole, the size of the organ, as of the entire organism, is directly proportional to the number and not to the size of the cells, just as in the mature individuals of *Crepidula*. The available data are, however, too scanty to justify any very positive conclusions, and it is probable that further experiment will disclose factors at present unknown. It would be highly interesting to determine whether such dwarf embryos could in the end restore the normal number of cells, and, hence, the normal size of the body. In all the cases thus far determined the dwarf gastrulas give rise to larvæ (*Plutei*, etc.) correspondingly dwarfed; but their later history has not yet been sufficiently followed out.

The gradual diminution of the energy of division during development by no means proceeds at a uniform pace in all of the cells, and, during the cleavage, the individual blastomeres are often found to exhibit entirely different rhythms of division, periods of active division being succeeded by long pauses, and sometimes by an entire cessa-

---

[1] See Amelung ('93) and Strasburger ('93).

tion of division even at a very early period. In the echinoderms, for example, it is well established that division suddenly pauses, or changes its rhythm, just before the gastrulation (in *Synapta* at the 512-cell stage, according to Selenka), and the same is said to be the case in *Amphioxus* (Hatschek, Lwoff). In *Nereis*, one of the blastomeres on each side of the body in the forty-two-cell stage suddenly ceases to divide, migrates into the interior of the body, and is converted into a unicellular glandular organ.[1] In the same animal, the four lower cells (macromeres) of the eight-cell stage divide in nearly regular succession up to the thirty-eight-cell stage, when a long pause takes place, and when the divisions are resumed they are of a character totally different from those of the earlier period. The cells of the ciliated belt or prototroch in this and other annelids likewise cease to divide at a certain period, their number remaining fixed thereafter.[2] Again, the number of cells produced for the foundation of particular structures is often definitely fixed, even when their number is afterward increased by division. In annelids and gasteropods, for example, the entire ectoblast arises from twelve micromeres segmented off in three successive quartets of micromeres from the blastomeres of the four-cell stage. Perhaps the most interesting numerical relations of this kind are those recently discovered in the division of teloblasts, where the number of divisions is directly correlated with the number of segments or somites. It is well known that this is the case in certain plants (*Characeæ*), where the alternating nodes and internodes of the stem are derived from corresponding single cells successively segmented off from the apical cell. Vejdovský's observations on the annelid *Dendrobæna* give strong ground to believe that the number of metamerically repeated parts of this animal, and probably of other annelids, corresponds in like manner with that of the number of cells segmented off from the teloblasts. The most remarkable and accurately determined case of this kind is that of the isopod crustacea, where the number of somites is limited and perfectly constant. In the embryos of these animals there are two groups of teloblasts near the hinder end of the embryo, viz. an inner group of mesoblasts, from which arise the mesoblast-bands, and an outer group of ectoblasts, from which arise the neural plates and the ventral ectoblast. McMurrich ('95) has recently demonstrated that the mesoblasts always divide exactly sixteen times, the ectoblasts thirty-two (or thirty-three) times, before relinquishing their teleoblastic mode of division and breaking up into smaller cells. Now the sixteen groups of cells thus formed give rise to the sixteen respective somites of the post-naupliar region of the embryo (*i.e.* from the second maxilla backward). In other words, each single division of the mesoblasts and each double division of the ectoblasts splits off the material for a single somite! The number of these divisions, and hence of the corresponding somites, is a fixed inheritance of the species.

---

[1] This organ, doubtfully identified by me as the head-kidney, is probably a mucus-gland (Mead).

[2] *Cf.* Fig. 171.

The causes that determine the rhythm of division, and thus finally establish the adult equilibrium, are but vaguely comprehended. The ultimate causes must of course lie in the inherited constitution of the organism, and are referable in the last analysis to the structure of the germ-cells. Every division must, however, be the response of the cell to a particular set of conditions or stimuli; and it is through the investigation of these stimuli that we may hope to penetrate farther into the nature of development. The immediate, specific causes of cell-division are still imperfectly known. In the adult, cells may be stimulated to divide by the utmost variety of agencies — by chemical stimulus, as in the formation of galls, or in hyperplasia induced by the injection of foreign substances into the blood; by mechanical pressure, as in the formation of calluses; by injury, as in the healing of wounds and in the regeneration of lost parts; and by a multitude of more complex physiological and pathological conditions, — by any agency, in short, that disturbs the normal equilibrium of the body. In all these cases, however, it is difficult to determine the *immediate stimulus* to division; for a long chain of causes and effects may intervene between the primary disturbance and the ultimate reaction of the dividing cells. Thus there is reason to believe that the formation of a callus is not directly caused by pressure or friction, but through the determination of an increased blood-supply to the part affected and a heightened nutrition of the cells. Cell-division is here probably incited by local chemical changes; and the opinion is gaining ground that the immediate causes of division, whatever their antecedents, are to be sought in this direction. That such is the case is indicated by nothing more clearly than the recent experiments on the egg by R. Hertwig, Mead, Morgan, and Loeb already referred to in part at pages 111 and 215. The egg-cell is, in most cases, stimulated to divide by the entrance of the spermatozoön, but in parthenogenesis exactly the same result is produced by an apparently quite different cause. The experiments in question give, however, ground for the conclusion that the common element in the two cases is a chemical stimulus. In the eggs of *Chætopterus* under normal conditions the first polar mitosis pauses at the anaphase until the entrance of the spermatozoön, when the mitotic activity is resumed and both polar bodies are formed. Mead ('98) shows, however, that the same effect may be produced without fertilization by placing the eggs for a few minutes in a weak solution of potassium chloride. In like manner R. Hertwig ('96) and Morgan ('99) show that unfertilized echinoderm-eggs may be stimulated to division by treatment with weak solution of strychnine, sodium-chloride, and other reagents, the result being here more striking than in the case of *Chætopterus*, since the entire mitotic system is formed anew under the chemical stimulus. The climax of these experiments is reached in Loeb's artificial production of parthenogenesis in sea-urchin eggs by treatment with dilute magnesium chloride. Beside these interesting results may be placed the remarkable facts of gall-formation in plants, which seem to leave no doubt that extremely complex and characteristic abnormal growths may result from specific chemical stimuli, and many pathologists have held that tumours and other pathological growths in the animal body may be incited through disturbances of circulation or other causes resulting in abnormal local chemical conditions.[1]

But while we have gained some light on the immediate causes of division, we have still to inquire how those causes are set in operation and are coördinated toward a typical end; and we are thus brought again to the general problem of growth. A very interesting suggestion is the resistance-theory of Thiersch and Boll, according to which each tissue continues to grow up to the limit afforded by the resistance of neighbouring tissues or organs. The removal or lessening of this resistance through injury or disease causes a resumption of growth and division, leading either to the regeneration of the lost parts or to the formation of abnormal growths. Thus the removal of a salamander's limb would seem to remove a barrier to the proliferation and growth of the remaining cells. These processes are therefore resumed, and continue until the normal barrier is reestablished by the regeneration. To speak of such a "barrier" or "resistance" is, however, to use a highly figurative phrase which is not to be construed in a rude mechanical sense. There is no doubt that hypertrophy, atrophy, or displacement of particular parts often leads to compensatory changes in the neighbouring parts; but it is equally certain that such changes are not a direct mechanical effect of the disturbance, but a highly complex physiological response to it. How complex the problem is, is shown by the fact that even closely related animals may differ widely in this respect. Thus Fraisse has shown that the salamander may completely regenerate an amputated limb, while the frog only heals the wound without further regeneration.[2] Again, in the case of cœlenterates, Loeb and Bickford have shown that the tubularian hydroids are able to regenerate the tentacles at both ends of a segment of the stem, while the polyp *Cerianthus* can regenerate them only at the distal end of a section (Fig. 194).

---

[1] *Cf.* p. 97. For a good discussion of this subject, see E. Ziegler, '89.

[2] In salamanders regeneration only takes place when the bone is cut across, and does not occur if the limb be exarticulated and removed at the joint.

In the latter case, therefore, the body possesses an inherent polarity which cannot be overturned by external conditions. A very curious case is that of the earthworm, which has long been known to possess a high regenerative capacity. If the posterior region of the worm be cut off, a new tail is usually regenerated. If the same operation be performed far forward in the anterior region, a new head is often formed at the front end of the posterior piece. If, however, the section be in the middle region the posterior piece sometimes regenerates a head, but more usually a tail, as was long since shown by Spallanzani and recently by Morgan ('99). Why such a blunder should be committed remains for the present quite unexplained.

It remains to inquire more critically into the nature of the correlation between growth and cell-division. In the growing tissues the direction of the division-planes in the individual cells evidently stands in a definite relation with the axes of growth in the body, as is especially clear in the case of rapidly elongating structures (apical buds, teloblasts, and the like), where the division-planes are predominantly transverse to the axis of elongation. Which of these is the primary factor, the direction of general growth or the direction of the division-planes? This question is a difficult one to answer, for the two phenomena are often too closely related to be disentangled. As far as the plants are concerned, however, it has been conclusively shown by Hofmeister, De Bary, and Sachs that *the growth of the mass is the primary factor;* for the characteristic mode of growth is often shown by the growing mass before it splits up into cells, and the form of cell-division adapts itself to that of the mass: "Die Pflanze bildet Zellen, nicht die Zelle bildet Pflanzen" (De Bary).

Much of the recent work in normal and experimental embryology, as well as that on regeneration, indicates that the same is true in principle of animal growth. Among recent writers who have urged this view should be mentioned Rauber, Hertwig, Adam Sedgwick, and especially Whitman, whose fine essay on the *Inadequacy of the Cell-theory of Development* ('93) marks a distinct advance in our point of view. Still more recently this view has been almost demonstrated through some remarkable experiments on regeneration, which show that definitely formed material, in some cases even the adult tissues, may be *directly moulded into new structures.* Driesch has shown ('95, 2, '99) that if gastrulas of *Sphærechinus* be bisected through the equator so that each half contains both ectoderm and entoderm, the wounds heal, each half forming a typical gastrula, in which the enteron differentiates itself into the three typical regions (fore, middle, and hind gut) correctly proportioned, though the whole structure is but half the normal size. Here, therefore, the formative process is in the main independent of cell-division or increase in size. Miss Bickford

('94) found that in the regeneration of decapitated hydranths of tubularians the new hydranth is primarily formed, not by new cell-formation and growth from the cut end, but by direct transformation of the distal portion of the stem.[1] Morgan's remarkable observations on *Planaria*, finally, show that here also, when the animal is cut into pieces, complete animals are produced from these pieces, but only in small degree through the formation of new tissue, and mainly by direct remoulding of the old material into a new body having the correct proportions of the species. As Driesch has well said, it is as if a plan or mould of the new little worm were first prepared and then the old material were poured into it.[2]

Facts of this kind, of which a considerable store has been accumulated, give strong ground for the view that cell-formation is subordinate to growth, or rather to the general formative process of which growth is an expression; and they furnish a powerful argument against Schwann's conception of the organism as a cell-composite (p. 58). That conception is, however, not to be rejected *in toto*, but contains a large element of truth; for there are many cases in which cells possess so high a degree of independence that profound modifications may occur in special regions through injury or disease, without affecting the general equilibrium of the body. The most striking proof of this lies in the fact that grafts or transplanted structures may perfectly retain their specific character, though transferred to a different region of the body, or even to another species. Nevertheless the facts of regeneration prove that even in the adult the formative processes in special parts are in many cases definitely correlated with the organization of the entire mass; and there is reason to conclude that such a correlation is a survival, in the adult, of a condition characteristic of the embryonic stages, and that the independence of special parts in the adult is a secondary result of development. The study of cell-division thus brings us finally to a general consideration of development which forms the subject of the following chapter.

LITERATURE. VIII

Berthold, G. — Studien über Protoplasma-mechanik. *Leipzig*, 1886.

Boll, Fr. — Das Princip des Wachsthums. *Berlin*, 1876.

Bourne, G. C. — A Criticism of the Cell-theory; being an answer to Mr. Sedgwick's article on the Inadequacy of the Cellular Theory of Development: *Quart. Journ. Mic. Sci.*, XXXVIII. 1. 1895.

---

[1] Driesch suggests for such a process the term *reparation* in contradistinction to true regeneration.

[2] '99, p. 55. It is mainly on these considerations that Driesch ('99) has built his recent theory of vitalism (*cf.* p. 417), the nature of the formative power being regarded as a problem *sui generis*, and one which the "machine-theory of life" is powerless to solve. *Cf.* also the views of Whitman, p. 416.

Castle, W. E. — The early Embryology of Ciona. *Bull. Mus. Comp. Zoöl.*, XXVII. 1896.

Conklin, E. G. — The Embryology of *Crepidula: Journ. Morph.*, XIII. 1897.

Driesch, H. — (See Literature, IX.)

Errera, L. — Zellformen und Seifenblasen: *Tagebl. der 60 Versammlung deutscher Naturforscher und Aerzte zu Wiesbaden.* 1887.

Hertwig, O. — Das Problem der Befruchtung und der Isotropie des Eies, eine Theorie der Vererbung. *Jena*, 1884.

Hofmeister. — Die Lehre von der Pflanzenzelle. *Leipzig*, 1867.

Jennings, H. S. — The Early Development of Asplanchna: *Bull. Mus. Comp. Zoöl.*, XXX. 1. *Cambridge*, 1896.

Kofoid, C. A. — On the Early Development of Limax: *Bull. Mus. Comp. Zoöl.*, XXVII. 1895.

Lillie, F. R. — The Embryology of the Unionidæ: *Journ. Morph.*, X. 1895.

Id. — Adaptation in Cleavage: *Wood's Holl Biol. Lectures.* 1899.

McMurrich, J. P. — Embryology of the Isopod Crustacea: *Journ. Morph.*, XI. 1. 1895.

Mark, E. L. — Limax. (See list IV.)

Morgan, T. H. — (See Literature, IX.)

Rauber, A. — Neue Grundlegungen zur Kenntniss der Zelle: *Morph. Jahrb.*, VIII. 1883.

Rhumbler, L. — Allgemeine Zellmechanik: *Merkel u. Bonnet, Ergeb.*, VIII. 1898.

Sachs, J. — Pflanzenphysiologie. (See list VII.)

Sedgwick, H. — On the Inadequacy of the Cellular Theory of Development, etc.: *Quart. Journ. Mic. Sci.*, XXXVII. 1. 1894.

Strasburger, E. — Über die Wirkungssphäre der Kerne und die Zellgrösse: *Histologische Beiträge*, V. 1893.

Zur Strassen, O. — Embryonalentwickelung der Ascaris: *Arch. Entom.*, III. 1896.

Watasé, S. — Studies on Cephalopods; I., Cleavage of the Ovum: *Journ. Morph.*, IV. 3. 1891.

Whitman, C. O. — The Inadequacy of the Cell-theory of Development: *Wood's Holl Biol. Lectures.* 1893.

Wilson, Edm. B. — The Cell-lineage of *Nereis: Journ. Morph.*, VI. 3. 1892.

Id. — Amphioxus and the Mosaic Theory of Development: *Journ. Morph.*, VIII. 3. 1893.

Id. — Considerations on Cell-lineage and Ancestral Reminiscence: *Ann. N. Y. Acad.*, XI. 1898; also *Wood's Holl Biol. Lectures*, 1899.

CHAPTER IX

THEORIES OF INHERITANCE AND DEVELOPMENT

"It is certain that the germ is not merely a body in which life is dormant or potential, but that it is itself simply a detached portion of the substance of a preëxisting living body."
HUXLEY.[1]

"Inheritance must be looked at as merely a form of growth." DARWIN.[2]

"Ich möchte daher wohl den Versuch wagen, durch eine Darstellung des Beobachteten Sie zu einer tiefern Einsicht in die Zeugungs- und Entwickelungsgeschichte der organischen Körper zu führen und zu zeigen, wie dieselben weder vorgebildet sind, noch auch, wie man sich gewöhnlich denkt, aus ungeformter Masse in einem bestimmten Momente plötzlich ausschiessen."
VON BAER.[3]

EVERY discussion of inheritance and development must take as its point of departure the fact that the germ is a single cell similar in its essential nature to any one of the tissue-cells of which the body is composed. That a cell can carry with it the sum total of the heritage of the species, that it can in the course of a few days or weeks give rise to a mollusk or a man, is the greatest marvel of biological science. In attempting to analyze the problems that it involves, we must from the outset hold fast to the fact, on which Huxley insisted, that the wonderful formative energy of the germ is not impressed upon it from without, but is inherent in the egg as a heritage from the parental life of which it was originally a part. The development of the embryo is nothing new. It involves no breach of continuity, and is but a continuation of the vital processes going on in the parental body. What gives development its marvellous character is the rapidity with which it proceeds and the diversity of the results attained in a span so brief.

But when we have grasped this cardinal fact, we have but focussed our instruments for a study of the real problem. *How* do the adult characteristics lie latent in the germ-cell; and how do they become patent as development proceeds? This is the final question that looms in the background of every investigation of the cell. In approaching it we may well make a frank confession of ignorance; for in spite of all that the microscope has revealed, we have not yet penetrated the mystery, and inheritance and development still remain in their fundamental aspects as great a riddle as they were to the Greeks. What we have gained is a tolerably precise acquaintance with the external aspects of development. The gross errors of the early preformationists have been dispelled.[1] We know that the germ-cell contains no predelineated embryo; that development is manifested, on the one hand, by the cleavage of the egg, on the other hand, by a process of differentiation, through which the products of cleavage gradually assume diverse forms and functions, and so accomplish a physiological division of labour. We can clearly recognize the fact that these processes fall in the same category as those that take place in the tissue-cells; for the cleavage of the ovum is a form of mitotic cell-division, while, as many eminent naturalists have perceived, differentiation is nearly related to growth and has its root in the phenomena of nutrition and metabolism. The real problem of development is *the orderly sequence and correlation of these phenomena toward a typical result.* We cannot escape the conclusion that this is the outcome of the organization of the germ-cells; but the nature of that which, for lack of a better term, we call "organization," is and doubtless long will remain almost wholly in the dark.

---

[1] *Evolution, Science and Culture*, p. 291.

[2] *Variation of Animals and Plants*, II., p. 398.

[3] *Entwick. der Thiere*, II., 1837, p. 8.

In the following discussion, which is necessarily compressed within narrow limits, we shall disregard the earlier baseless speculations, such as those of the seventeenth and eighteenth centuries, which attempted a merely formal solution of the problem, confining ourselves to more recent discussions that have grown directly out of modern research. An introduction to the general subject may be given by a preliminary examination of two central hypotheses about which most recent discussions have revolved. These are, first, the theory of *Germinal Localization*[2] of Wilhelm His ('74), and, second, the *Idioplasm Hypothesis* of Nägeli ('84). The relation between these two conceptions, close as it is, is not at first sight very apparent; and for the purpose of a preliminary sketch they may best be considered separately.

A. The Theory of Germinal Localization

Although the *naïve* early theory of preformation and evolution was long since abandoned, yet we find an after-image of it in the theory of germinal localization which in one form or another has been advocated by some of the foremost students of development. It is maintained that, although the embryo is not pre*formed* in the germ, it must nevertheless be pre*determined* in the sense that the egg contains definite areas or definite substances predestined for the formation of corresponding parts of the embryonic body. The first clear statement of this conception is found in the interesting and suggestive work of Wilhelm His ('74) entitled *Unsere Körperform.* Considering the development of the chick, he says: "It is clear, on the one hand, that every point in the embryonic region of the blastoderm must represent a later organ or part of an organ, and, on the other hand, that every organ developed from the blastoderm has its preformed germ (vorgebildete Anlage) in a definitely located region of the flat germ-disc. . . . The material of the germ is already present in the flat germ-disc, but is not yet morphologically marked off and hence not directly recognizable. But by following the development backwards we may determine the location of every such germ, even at a period when the morphological differentiation is incomplete or before it occurs; logically, indeed, we must extend this process back to the fertilized or even the unfertilized egg. According to this principle, the germ-disc contains the organ-germs spread out in a flat plate, and, conversely, every point of the germ-disc reappears in a later organ; I call this the *principle of organ-forming germ-regions.*"[1] His thus conceived the embryo, not as pre*formed*, but as having all of its parts pre*localized* in the egg-protoplasm (cytoplasm).

---

[1] *Cf.* Introduction, p. 8.

[2] I venture to suggest this term as an English equivalent for the awkward expression "Organbildende Keimbezirke" of His.

A great impulse to this conception was given during the following decade by discoveries relating, on the one hand, to protoplasmic structure, on the other hand, to the promorphological relations of the ovum. Ray Lankester writes, in 1877: "Though the substance of a cell[2] may appear homogeneous under the most powerful microscope, it is quite possible, indeed certain, that it may contain, *already formed and individualized*, various kinds of physiological molecules. The visible process of segregation is only the sequel of a differentiation already established, and not visible."[3] The egg-cytoplasm has a definite molecular organization directly handed down from the parent; cleavage sunders the various "physiological molecules" and isolates them in particular cells. Whitman expresses a similar thought in the following year: "While we cannot say that the embryo is predelineated, we can say that it is predetermined. The 'histogenetic sundering' of embryonic elements begins with the cleavage, and every step in the process bears a definite and invariable relation to antecedent and subsequent steps. . . . It is, therefore, not surprising to find certain important histological differentiations and fundamental structural relations anticipated in the early phases of cleavage, and foreshadowed even before cleavage begins."[4] It was, however, Flemming who gave the first specific statement of the matter from the cytological point of view: "But if the substance of the egg-cell has a definite *structure* (Bau), and if this structure and the nature of the network varies in different regions of the cell-body, we may seek in it a basis for the predetermination of development wherein one egg differs from another, and it will be possible to look for it *with the microscope*. How far this search can be carried no one can say, but its ultimate aim is nothing less than a true *morphology of inheritance*."[1] In the following year Van Beneden pointed out how nearly this conception approaches to a theory of preformation: "If this were the case (*i.e.* if the egg-axis coincided with the principal axis of the adult body), the old theory of evolution would not be as baseless as we think to-day. The fact that in the ascidians, and probably in other bilateral animals, the median plane of the body of the future animal is marked out from the beginning of cleavage, fully justifies the hypothesis that the materials destined to form the right side of the body are situated in one of the lateral hemispheres of the egg, while the left hemisphere gives rise to all of the organs of the left half."[2]

---

[1] *l. c.*, p. 19.

[2] It is clear from the context that by "substance" Lankester had in mind the cytoplasm, though this is not specifically stated.

[3] '77, p. 14.

[4] '78, p. 49.

The hypothesis thus suggested seemed, for a time, to be placed on a secure basis of fact through a remarkable experiment subsequently performed by Roux ('88) on the frog's egg. On killing one of the blastomeres of the two-cell stage by means of a heated needle the uninjured half developed in some cases into a well-formed half-larva (Fig. 182), representing approximately the right or left half of the body, containing one medullary fold, one auditory pit, etc.[3] Analogous, though less complete, results were obtained by operating with the four-cell stage. Roux was thus led to the declaration (made with certain subsequent reservations) that "the development of the frog-gastrula and of the embryo formed from it is from the second cleavage onward a mosaic-work, consisting of at least four vertical independently developing pieces."[4] This conclusion seemed to form a very strong support to His's theory of germinal localization, though, as will appear beyond, Roux transferred this theory to the nucleus, and thus developed it in a very different direction from Lankester or Van Beneden. His's theory also received very strong apparent support through investigations on cell-lineage by Whitman, Rabl, and many later observers, which have shown that in the cleavage of annelids, mollusks, platodes, tunicates, and many other animals, every cell has a definite origin and fate, and plays a definite part in the building of the body.[1]

---

[1] Zellsubstanz, '82, p. 70: the italics are in the original.

[2] '83, p. 571.

[3] The accuracy of this result was disputed by Oscar Hertwig ('93, 1), who found that the uninjured blastomere gave rise to a defective larva, in which certain parts were missing, but not to a true half-body. Later observers, especially Schultze, Endres, and Morgan, have, however, shown that both Hertwig and Roux were right, proving that the uninjured blastomere may give rise to a true half-larva, to a larva with irregular defects, or to a whole larva of half-size, according to circumstances (p. 422).

[4] *l.c.*, p. 30.

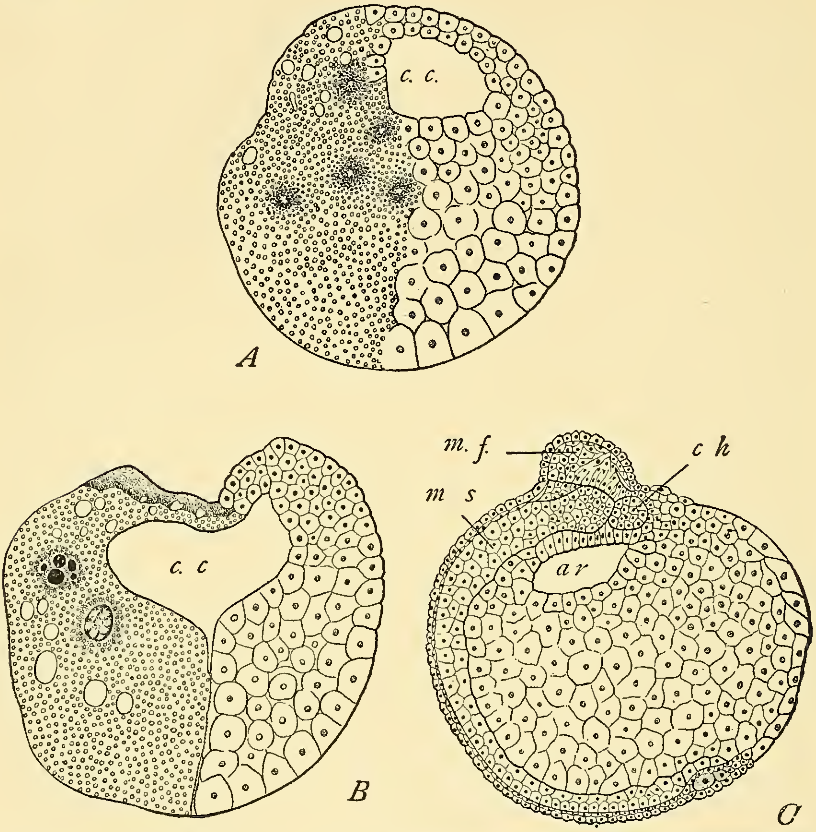

Fig. 182. — Half-embryos of the frog (in transverse section) arising from a blastomere of the two-cell stage after killing the other blastomere. [ROUX.]

A. Half-blastula (dead blastomere on the left). *B*. Later stage. *C*. Half-tadpole with one medullary fold and one mesoblast plate; regeneration of the missing (right) half in process.

ar. archenteric cavity; *c.c.* cleavage-cavity; *ch*. notochord; *m.f.* medullary fold; *m.s.* mesoblast-plate.

In an able series of later works Whitman has followed out the suggestion made in his paper of 1878, cited above, pointing out how essential a part is played in development by the cytoplasm and insisting that cytoplasmic preorganization must be regarded as a leading factor in the ontogeny. Whitman's interesting and suggestive views are expressed with great caution and with a full recognition of the difficulty and complexity of the problem. From his latest essay, indeed ('94), it is not easy to gather his precise position regarding the theory of cytoplasmic localization. Through all his writings, nevertheless, runs the leading idea that the germ is definitely organized before development begins, and that cleavage only reveals an organization that exists from the beginning. "That organization precedes cell-formation and regulates it, rather than the reverse, is a conclusion that forces itself upon us from many sides."[1] "The organism exists before cleavage sets in, and persists throughout every stage of cell-multiplication."[2]

---

[1] *Cf.* p. 378.

All of these views, excepting those of Roux, lean more or less distinctly toward the conclusion that the cytoplasm of the egg-cell is from the first mapped out, as it were, into regions which correspond with the parts of the future embryonic body. The cleavage of the ovum does not create these regions, but only reveals them to view by marking off their boundaries. Their topographical arrangement in the egg does not necessarily coincide with that of the adult parts, but only involves the latter as a necessary consequence — somewhat as a picture in the kaleidoscope gives rise to a succeeding picture composed of the same parts in a different arrangement. The germinal localization may, however, in a greater or less degree, foreshadow the arrangement of adult parts — for instance, in the egg of the tunicate or cephalopod, where the bilateral symmetry and antero-posterior differentiation of the adult is foreshadowed not only in the cleavage stages, but even in the unsegmented egg.

By another set of writers, such as Roux, De Vries, Hertwig, and Weismann, germinal localization is primarily sought not in the cytoplasm, but in the nucleus; but these views can be best considered after a review of the idioplasm hypothesis, to which we now proceed.

B. THE IDIOPLASM THEORY

We owe to Nägeli the first systematic attempt to discuss heredity regarded as inherent in a definite physical basis;[3] but it is hardly necessary to point out his great debt to earlier writers, foremost among them Darwin, Herbert Spencer, and Häckel. The essence of Nägeli's hypothesis was the assumption that inheritance is effected by the transmission not of a cell, considered as a whole, but of a particular substance, the *idioplasm*, contained within a cell, and forming the physical basis of heredity. The idioplasm is to be sharply distinguished from the other constituents of the cell, which play no direct part in inheritance and form a "nutritive plasma" or *tropho-*

---

[1] '93, p. 115.

[2] *l.c.*, p. 112.

[3] *Theorie der Abstammungslehre*, 1884.

plasm. Hereditary traits are the outcome of a definite molecular organization of the idioplasm. The hen's egg differs from the frog's because it contains a different idioplasm. The species is as completely contained in the one as in the other, and the hen's egg differs from a frog's egg as widely as a hen from a frog.

The idioplasm was conceived as an extremely complex substance, consisting of elementary complexes of molecules known as *micellæ*. These are variously grouped to form units of higher orders, which, as development proceeds, determine the development of the adult cells, tissues, and organs. The specific peculiarities of the idioplasm are therefore due to the arrangement of the micellæ; and this, in its turn, is owing to dynamic properties of the micellæ themselves. During development the idioplasm undergoes a progressive transformation of its substance, not through any material change, but through dynamic alterations of the conditions of tension and movement of the micellæ. These changes in the idioplasm cause reactions on the part of surrounding structures leading to definite chemical and plastic changes, *i.e.* to differentiation and development.

Nägeli made no attempt to locate the idioplasm precisely or to identify it with any of the known morphological constituents of the cell. It was somewhat vaguely conceived as a network extending through both nucleus and cytoplasm, and from cell to cell throughout the entire organism. Almost immediately after the publication of his theory, however, several of the foremost leaders of biological investigation were led to locate the idioplasm in the nucleus, and concluded that it is to be identified with *chromatin*. The grounds for this conclusion, which have already been stated in Chapter VII., may be here again briefly reviewed. The beautiful experiments of Nussbaum, Gruber, and Verworn proved that the regeneration of differentiated cytoplasmic structures in the Protozoa can only take place when nuclear matter is present (*cf.* p. 342). The study of fertilization by Hertwig, Strasburger, and Van Beneden proved that in the sexual reproduction of both plants and animals the nucleus of the germ is equally derived from both sexes, while the cytoplasm is derived almost entirely from the female. The two germ-nuclei, which by their union give rise to that of the germ, were shown by Van Beneden to be of exactly the same morphological nature, since each gives rise to chromosomes of the same number, form, and size. Van Beneden and Boveri proved (p. 182) that the paternal and maternal nuclear substances are equally distributed to each of the first two cells, and the more recent work of Häcker, Rückert, Herla, and Zoja establishes a strong probability that this equal distribution continues in the later divisions. Roux pointed out the telling fact that the entire complicated mechanism of mitosis seems designed to affect the most accurate division of the entire nuclear substance in all of its parts, while fission of the cytoplasmic cell-body is in the main a mass-division, and not a meristic division of the individual parts. Again, the complicated processes of maturation show the significant fact that while the greatest pains is taken to prepare the germ-nuclei for their coming union, by rendering them exactly equivalent, the cytoplasm becomes widely different in the two germ-cells and is devoted to entirely different functions.

It was in the main these considerations that led Hertwig, Strasburger, Kölliker, and Weismann independently and almost simultaneously to the conclusion that *the nucleus contains the physical basis of inheritance, and that chromatin, its essential constituent, is the idioplasm postulated in Nägeli's theory.* This conclusion is now widely accepted and rests upon a basis so firm that it must be regarded as a working hypothesis of high value. To accept it is, however, to reject the theory of germinal localization in so far as it assumes a prelocalization of the egg-cytoplasm as a fundamental character of the egg. For if the specific character of the organism be determined by an idioplasm contained in the chromatin, then every characteristic of the cytoplasm must in the long run be determined from the same source. A striking illustration of this point is given by the phenomena of colour-inheritance in plant-hybrids, as De Vries has pointed out. Pigment is developed in the embryonic cytoplasm, which is derived from the mother-cell; yet in hybrids it may be inherited from the male through the nucleus of the germ-cell. The specific form of cytoplasmic metabolism by which the pigment is formed must therefore be determined by the paternal chromatin in the germ-nucleus, and not by a predetermination of the egg-cytoplasm.

C. UNION OF THE TWO THEORIES

We have now to consider the attempts that have been made to transfer the localization-theory from the cytoplasm to the nucleus, and thus to bring it into harmony with the theory of nuclear idioplasm. These attempts are especially associated with the names of Roux, De Vries, Weismann, and Hertwig; but all of them may be traced back to Darwin's celebrated hypothesis of pangenesis as a prototype. This hypothesis is so well known as to require but a brief review. Its fundamental postulate assumes that the germ-cells contain innumerable ultra-microscopic organized bodies or *gemmules*, each of which is the germ of a cell and determines the development of a similar cell during the ontogeny. The germ-cell is, therefore, in Darwin's words, a microcosm formed of a host of inconceivably minute self-propagating organisms, every one of which predetermines the formation of one of the adult cells. De Vries ('89) brought this conception into relation with the theory of nuclear idioplasm by assuming that the gemmules of Darwin, which he called *pangens*, are contained in the nucleus, migrating thence into the cytoplasm step by step during ontogeny, and thus determining the successive stages of development. The hypothesis is further modified by the assumption that the pangens are not cell-germs, as Darwin assumed, but ultimate protoplasmic units of which cells are built, and which are the bearers of particular hereditary qualities. The same view was afterward accepted by Hertwig and Weismann.[2]

The theory of germinal localization is thus transferred from the cytoplasm to the nucleus. It is not denied that the egg-cytoplasm may be more or less distinctly differentiated into regions that have a constant relation to the parts of the embryo. This differentiation is, however, conceived, not as a primordial characteristic of the egg, but as one secondarily determined through the influence of the nucleus. Both De Vries and Weismann assume, in fact, that the entire cytoplasm is a product of the nucleus, being composed of pangens that migrate out from the latter, and by their active growth and multiplication build up the cytoplasmic substance.[3]

D. THE ROUX-WEISMANN THEORY OF DEVELOPMENT

We now proceed to an examination of two sharply opposing hypotheses of development based on the theory of nuclear idioplasm. One of these originated with Roux ('83) and has been elaborated especially by Weismann. The other was clearly outlined by De Vries ('89), and has been developed in various directions by Oscar Hertwig, Driesch, and other writers. In discussing them, it should be borne in mind that, although both have been especially developed by the advocates of the pangen-hypothesis, neither necessarily involves that hypothesis in its strict form, *i.e.* the postulate of discrete self-propagating units in the idioplasm. This hypothesis may therefore be laid

---

[1] *Cf.* p. 290.

[2] The neo-pangenesis of De Vries differs from Darwin's hypothesis in one very important respect. Darwin assumed that the gemmules arose in the body, being thrown off as germs by the individual tissue-cells, transported to the germ-cells, and there accumulated as in a reservoir; and he thus endeavoured to explain the transmission of acquired characters. De Vries, on the other hand, denies such a transportal from cell to cell, maintaining that the pangens arise or preëxist in the germ-cell, and those of the tissue-cells are derived from this source by cell-division.

[3] This conception obviously harmonizes with the *rôle* of the nucleus in the synthetic process. In accepting the view that the nuclear control of the cell is effected by an emanation of specific substances from the nucleus, we need not, however, necessarily adopt the pangen-hypothesis.

aside as an open question,[1] and will be considered only in so far as it is necessary to a presentation of the views of individual writers.

The Roux-Weismann hypothesis has already been touched on at page 245. Roux conceived the idioplasm (*i.e.* the chromatin) not as a single chemical compound or a homogeneous mass of molecules, but as a highly complex mixture of different substances, representing *different qualities*, and having their seat in the individual chromatin-granules. In mitosis these become arranged in a linear series to form the spireme-thread, and hence may be precisely divided by the splitting of the thread. Roux assumes, as a fundamental postulate, that division of the granules may be either *quantitative* or *qualitative*. In the first mode the group of qualities represented in the mother-granule is first doubled and then split into equivalent daughter-groups, the daughter-cells therefore receiving the same qualities and remaining of the same nature. In "qualitative division," on the other hand, the mother-group of qualities is split into dissimilar groups, which, passing into the respective daughter-nuclei, lead to *a corresponding differentiation in the daughter-cells*. By qualitative divisions, occurring in a fixed and predetermined order, the idioplasm is thus split up during ontogeny into its constituent qualities, which are, as it were, sifted apart and distributed to the various nuclei of the embryo. *Every cell-nucleus, therefore, receives a specific form of chromatin* which determines the nature of the cell at a given period and its later history. Every cell is thus endowed with a power of *self-determination*, which lies in the specific structure of its nucleus, and its course of development is only in a minor degree capable of modification through the relation of the cell to its fellows (" correlative differentiation ").

Roux's hypothesis, be it observed, does not commit him to the theory of pangenesis. It was reserved for Weismann to develop the hypothesis of qualitative division in terms of the pangen-hypothesis, and to elaborate it as a complete theory of development. In his first essay ('85), published before De Vries's paper, he went no farther than Roux. "I believe that we must accept the hypothesis that in indirect nuclear division, the formation of non-equivalent halves may take place quite as readily as the formation of equivalent halves, and that the equivalence or non-equivalence of the subsequently produced daughter-cells must depend upon that of the nuclei. Thus, during ontogeny a gradual transformation of the nuclear substance takes place, necessarily imposed upon it, according to certain laws, by its own nature, and such transformation is accompanied by a gradual change in the character of the cell-bodies."[2] In later writings Weismann advanced far beyond this, building up an elaborate artificial system, which appears in its final form in the remarkable

[1] *Cf.* Chapter VI.

[2] Essay IV., p. 193, 1885.

book on the germ-plasm ('92). Accepting De Vries's conception of the pangens, he assumes a definite grouping of these bodies in the germ-plasm or idioplasm (chromatin), somewhat as in Nägeli's conception. The pangens or *biophores* are conceived to be successively aggregated in larger and larger groups; namely, (1) *determinants*, which are still beyond the limits of microscopical vision; (2) *ids*, which are identified with the visible chromatin-granules; and (3) *idants*, or chromosomes. The chromatin has, therefore, a highly complex fixed architecture, which is transmitted from generation to generation, and determines the development of the embryo in a definite and specific manner. Mitotic division is conceived as an apparatus which may distribute the elements of the chromatin to the daughter-nuclei either equally or unequally. In the former case ("*homœokinesis*," *integral* or *quantitative division*), the resulting nuclei remain precisely equivalent. In the second case ("*heterokinesis*," *qualitative* or *differential division*), the daughter-cells receive different groups of chromatin-elements, and hence become differently modified. During ontogeny, through successive qualitative divisions, the elements of the idioplasm or *germ-plasm* (chromatin) are gradually sifted apart, and distributed in a definite and predetermined manner to the various parts of the body. "Ontogeny depends on a gradual process of disintegration of the id of germ-plasm, which splits into smaller and smaller groups of determinants in the development of each individual. . . . Finally, if we neglect possible complications, only *one* kind of determinant remains in each cell, viz. that which has to control that particular cell or group of cells. . . . In this cell it breaks up into its constituent biophores, and gives the cell its inherited specific character."[1] Development is, therefore, essentially evolutionary and not epigenetic;[2] its point of departure is a substance in which all of the adult characters are represented by preformed, prearranged germs; its course is the result of a predetermined harmony in the succession of the qualitative divisions by which the hereditary substance is progressively disintegrated. In order to account for heredity through successive generations, Weismann is obliged to assume that, by means of quantitative or integral division, a certain part of the original germ-plasm is carried on unchanged, and is finally delivered, with its original architecture unaltered, to the germ-nuclei. The power of regeneration is explained, in like manner, as the result of a transmission of unmodified or slightly modified germ-plasm to those parts capable of regeneration.

[1] *Germ-plasm*, pp. 76, 77.

[2] *l.c.*, p. 15.

E. CRITIQUE OF THE ROUX-WEISMANN THEORY

It is impossible not to admire the thoroughness, candour, and logical skill with which Weismann has developed his theory, or to deny that, in its final form, it does afford up to a certain point a *formal* solution of the problems with which it deals. Its fundamental weakness is its *quasi*-metaphysical character, which, indeed, almost places it outside the sphere of legitimate scientific hypothesis. Save in the maturation of the germ-cells ("reducing divisions"), none of the visible phenomena of cell-division give even a remote suggestion of qualitative division. All the facts of ordinary mitosis, on the contrary, indicate that the division of the chromatin is carried out with the most exact equality.

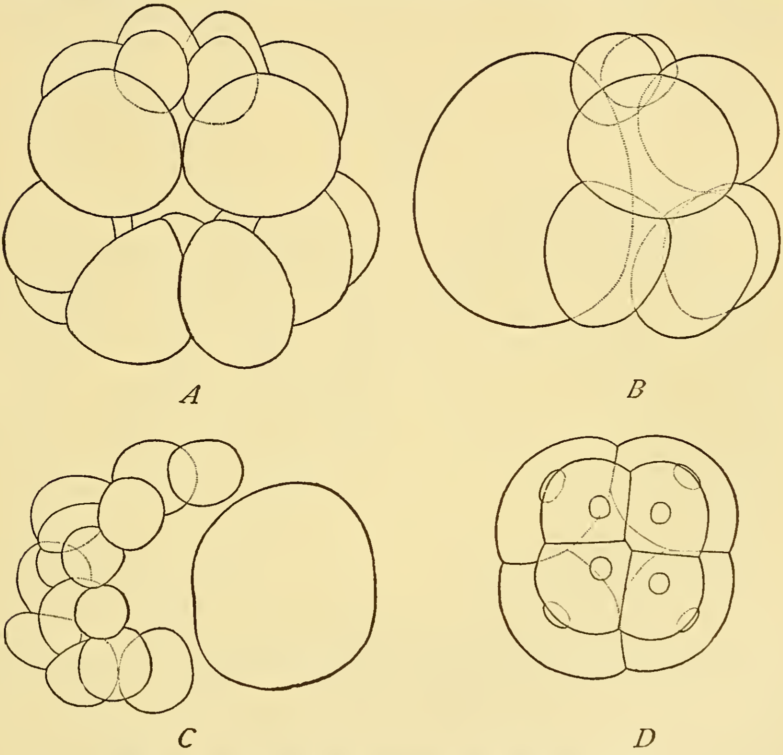

Fig. 183. — Half and whole cleavage in the eggs of sea-urchins.

A. Normal sixteen-cell stage, showing the four micromeres above (from Driesch, after Selenka). *B*. Half sixteen-cell stage developed from one blastomere of the two-cell stage after killing the other by shaking (Driesch). *C*. Half blastula resulting, the dead blastomere at the right (Driesch). *D*. Half-sized sixteen-cell stage of *Toxopneustes*, viewed from the micromere-pole (the eight lower not shown). This embryo, developed from an isolated blastomere of the two-cell stage, segmented like an entire normal ovum.

The hypothesis mainly rests upon a quite different order of phenomena, namely, on facts indicating that isolated blastomeres, or other cells, have a certain power of self-determination, or "self-differentiation" (Roux), peculiar to themselves, and which is assumed to be primarily due to the specific quality of the nuclei. This assumption, which may or may not be true,[1] is itself based upon the further assumption of qualitative nuclear division of which we actually know nothing whatever. The fundamental hypothesis is thus of purely *a priori* character; and every fact opposed to it has been met by subsidiary hypotheses, which, like their principal, relate to matters beyond the reach of observation.

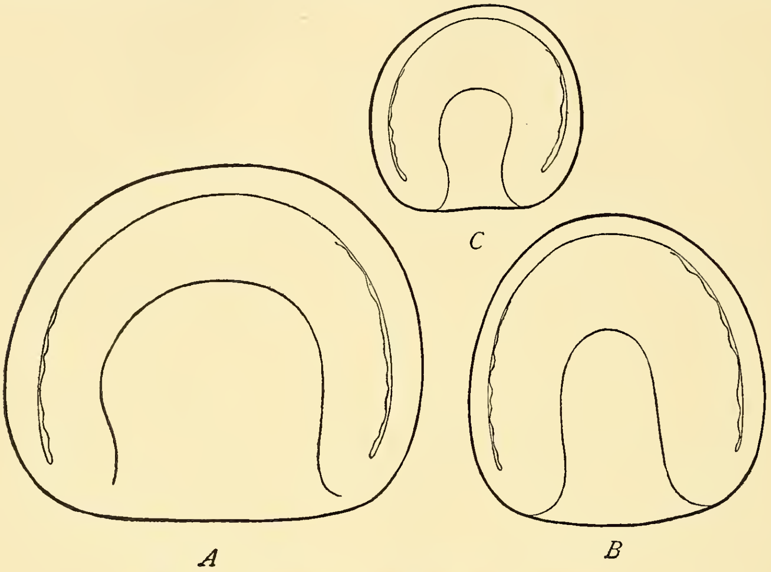

Fig. 184. — Normal and dwarf gastrulas of *Amphioxus*.

A. Normal gastrula. *B*. Half-sized dwarf, from an isolated blastomere of the two-cell stage. *C*. Quarter-sized dwarf, from an isolated blastomere of the four-cell stage.

Such an hypothesis cannot be actually overturned by a direct appeal to fact. We can, however, make an indirect appeal, the results of which show that the hypothesis of qualitative division is not only so improbable as to lose all semblance of reality, but is in fact quite superfluous. It is rather remarkable that Roux himself led the way in this direction. In the course of his observations on the development of a half-embryo from one of the blastomeres of the two-cell stage of the frog's egg, he determined the significant fact that the half-embryo in the end *restores more or less completely*

---

[1] *Cf.* p. 426.

the missing half by a peculiar process, related to regeneration, which Roux designated as *post-generation.* Later studies showed that an isolated blastomere is able to give rise to a complete embryo in many other animals, sometimes developing in its earlier stages as though still forming part of a complete embryo ("partial development"), but in other cases developing directly into a complete dwarf embryo, as if it were an egg of diminished size. In 1891 Driesch was able to follow out the development of isolated blastomeres of sea-urchin

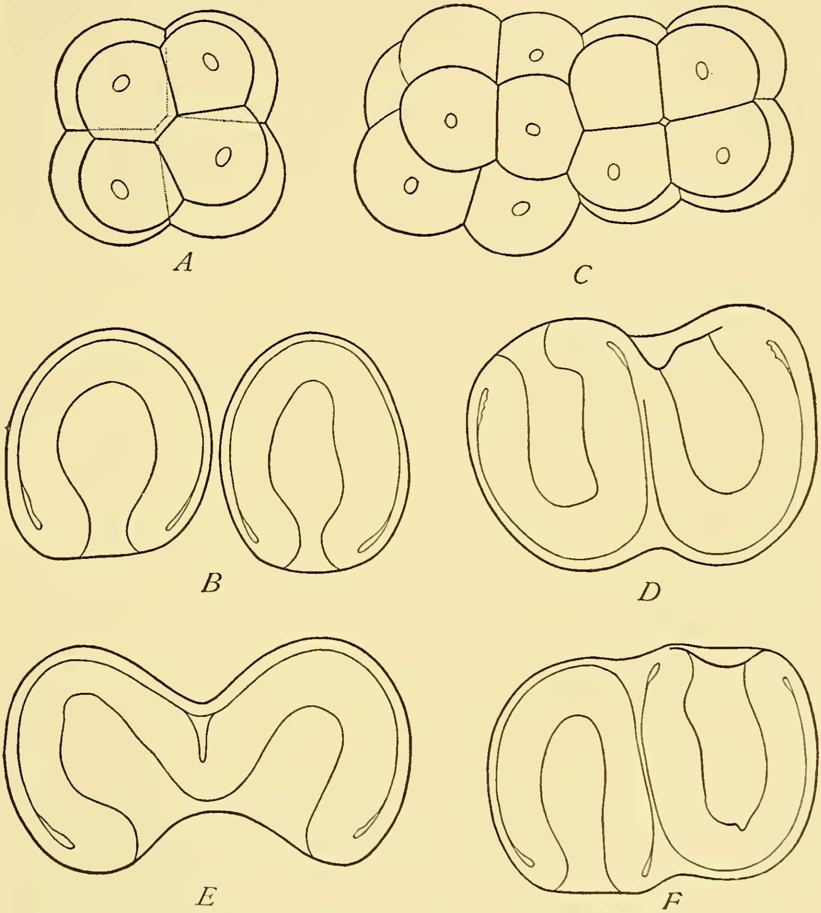

Fig. 185. — Dwarf and double embryos of *Amphioxus*.

A. Isolated blastomere of the two-cell stage segmenting like an entire egg (*cf.* Fig. 183, *D*). *B.* Twin gastrulas from a single egg. *C.* Double cleavage resulting from the partial separation, by shaking, of the blastomeres of the two-cell stage. *D.E.F.* Double gastrulas arising from such forms as the last.

eggs separated by shaking to pieces the two-cell and four-cell stages. Blastomeres thus isolated segment as if still forming part of an entire larva, and give rise to a half- (or quarter-) blastula (Fig. 183). The opening soon closes, however, to form a small complete blastula, and the resulting gastrula and Pluteus larva is a perfectly formed dwarf of only half (or quarter) the normal size. Incompletely separated blastomeres give rise to double embryos like the Siamese twins. Shortly afterward the writer obtained similar results in the case of *Amphioxus,* but here *the isolated blastomere behaves from the beginning like a complete ovum of half the usual size,* and gives rise to a complete blastula, gastrula, and larva. Complete embryos have also been obtained from a single blastomere in the teleost *Fundulus* (Morgan, '95, 2), in *Triton* (Herlitzka, '95), and in a number of hydromedusæ (Zoja, '95, Bunting, '99); and nearly complete embryos in the tunicates *Ascidiella* (Chabry, '87), *Phallusia* (Driesch, '94), and *Molgula* (Crampton, '98).[1] Perhaps the most striking of these cases is that of the hydroid *Clytia*, in which Zoja was able to obtain perfect embryos, not only from the blastomeres of the two-cell and four-cell stages, but from eight-cell and even from sixteen-cell stages, the dwarfs in the last case being but one-sixteenth the normal size.

These experiments render highly improbable the hypothesis of qualitative division in its strict form, for they demonstrate that the earlier cleavages, at least, do not in these cases sunder fundamentally different materials, either nuclear or cytoplasmic, but only split the egg up into a number of parts, each of which is capable of producing an entire body of diminished size, and hence must contain all of the material essential to complete development. Both Roux and Weismann endeavour to meet this adverse evidence with the assumption of a "reserve idioplasm," containing all of the elements of the germ-plasm which is in these cases distributed equally to all the cells in addition to the specific chromatin conveyed to them by qualitative division. This subsidiary hypothesis renders the principal one (*i.e.* that of qualitative division) superfluous, and brings us back to the same problems that arise when the assumption of qualitative division is discarded.

The theory of qualitative nuclear division has been practically disproved in another way by Driesch, through the pressure-experiments already mentioned at page 375. Following the earlier experiments of Pflüger ('84) and Roux ('85) on the frog's egg, Driesch subjected segmenting eggs of the sea-urchin to pressure, and thus obtained flat plates of cells in which the arrangement of the nuclei differed totally

---

[1] The "partial" development in the earlier stages of some of these forms is considered at page 419.

from the normal (Fig. 186); yet such eggs when released from pressure continue to segment, *without rearrangement of the nuclei*, and give rise to perfectly normal larvæ. I have repeated these experiments not only with sea-urchin eggs, but also with those of an annelid (*Nereis*), which yield a very convincing result, since in this case the histological differentiation of the cells appears very early. In the normal development of this animal the archenteron arises from four large cells or macromeres (entomeres), which remain after the successive formation of three quartets of micromeres (ectomeres) and the parent-cell of the mesoblast. After the primary differentiation of the germ-layers the four entomeres do not divide again until a very late period (free-swimming trochophore), and their substance always retains a characteristic appearance, differing from that of the other blastomeres in its pale non-granular character and in the presence of large oil-drops. If unsegmented eggs be subjected to pressure, as in Driesch's echinoderm experiments, they segment in a flat plate, all of the cleavages being vertical. In this way are formed eight-celled plates in which all of the cells contain oil-drops (Fig. 187, *D*). If they are now released from the pressure, each of the cells divides in a plane approximately horizontal, a smaller granular micromere being formed above, leaving below a larger clear macromere in which the oil-drops remain. The sixteen-cell stage, therefore, consists of eight deutoplasm-laden macromeres and eight protoplasmic micromeres (instead of four macromeres and twelve micromeres, as in the usual development). These embryos developed into free-swimming trochophores containing eight instead of four macromeres, which have the typical clear protoplasm containing oil-drops. In this case there can

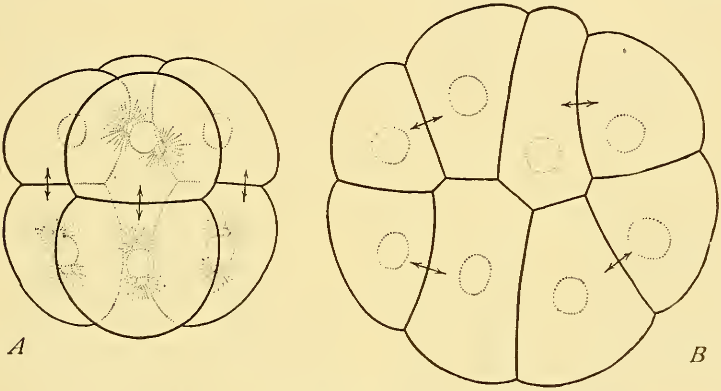

Fig. 186. — Modification of cleavage in sea-urchin eggs by pressure.

A. Normal eight-cell stage of *Toxopneustes*. *B*. Eight-cell stage of *Echinus* segmenting under pressure. Both forms produce normal Plutei.

be no doubt whatever that four of the entoblastic nuclei were normally destined for the first quartet of micromeres (Fig. 187, *B*), from which arise the apical ganglia and the prototroch. Under the conditions of the experiment, however, they have given rise to the nuclei of cells which differ in no wise from the other entoderm-cells. Even in a highly differentiated type of cleavage, therefore, the nuclei of the segmenting egg are not specifically different, as the Roux-Weismann hypothesis demands, but contain the same materials even in the cells that undergo the most diverse subsequent fate. But there is, furthermore, very strong reason for believing that this may be true in later

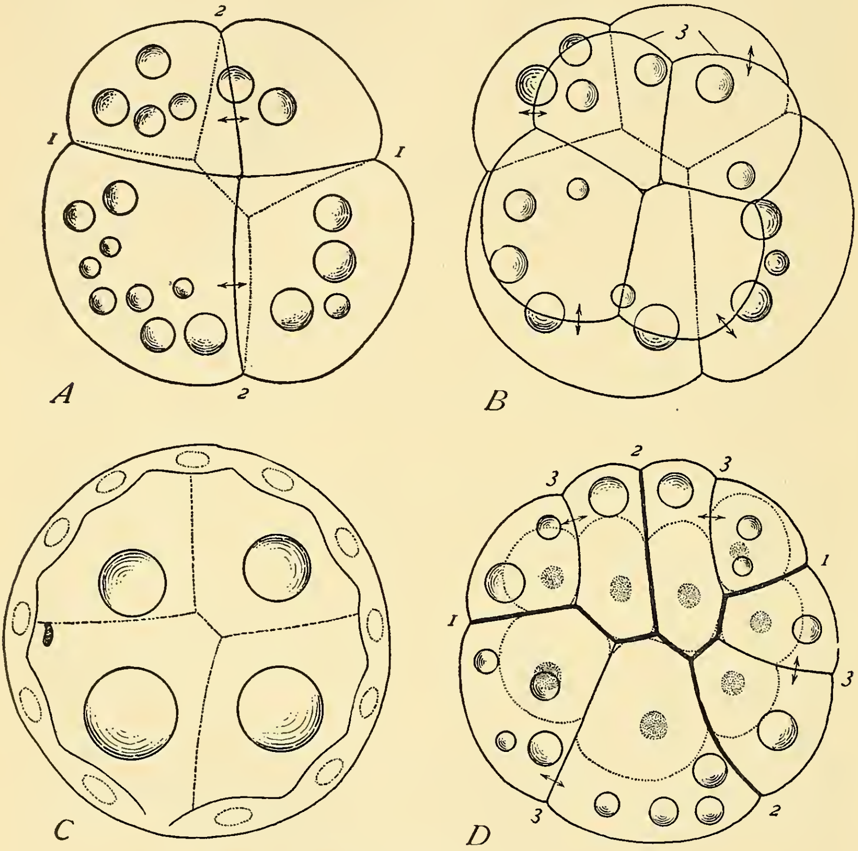

Fig. 187. — Modifications of cleavage by pressure in *Nereis*.

A. B. Normal four- and eight-cell stages. *C.* Normal trochophore larva resulting, with four entoderm-cells. *D.* Eight-cell stage arising from an egg flattened by pressure; such eggs give rise to trochophores with eight instead of four entoderm-cells. Numerals designate the successive cleavages.

stages as well, as Kölliker insisted in opposition to Weismann as early as 1886, and as has been urged by many subsequent writers. The strongest evidence in this direction is afforded by the facts of regeneration; and many cases are known — for instance, among the hydroids and the plants — in which even a small fragment of the body is able to reproduce the whole. It is true that the power of regeneration is always limited to a greater or less extent according to the species. But there is no evidence whatever that such limitation arises through specification of the nuclei by qualitative division, and, as will appear beyond, its explanation is probably to be sought in a very different direction.

F. On the Nature and Causes of Differentiation

We have now cleared the ground for a restatement of the problem of development and an examination of the views opposed to the Roux-Weismann theory. After discarding the hypothesis of qualitative division the problem confronts us in the following form. If chromatin be the idioplasm in which inheres the sum total of hereditary forces, and if it be equally distributed at every cell-division, how can its mode of action so vary in different cells as to cause diversity of structure, *i.e. differentiation?* It is perfectly certain that differentiation is an actual progressive transformation of the egg-substance involving both physical and chemical changes, occurring in a definite order, and showing a definite distribution in the regions of the egg. These changes are sooner or later accompanied by the cleavage of the egg into cells whose boundaries may sharply mark the areas of differentiation. What gives these cells their specific character? Why, in the four-cell stage of an annelid egg, should the four cells contribute equally to the formation of the alimentary canal and the cephalic nervous system, while only one of them (the left-hand posterior) gives rise to the nervous system of the trunk-region and to the muscles, connective tissues, and the germ-cells? (Figs. 171, 188, *B.*) There cannot be a fixed relation between the various regions of the egg which these blastomeres represent and the adult parts arising from them; for in some eggs these relations may be artificially changed. A portion of the egg which under normal conditions would give rise to only a fragment of the body will, if split off from the rest, give rise to an entire body of diminished size. What then determines the history of such a portion? What influence moulds it now into an entire body, now into a part of a body?

De Vries, in his remarkable essay on *Intracellular Pangenesis* ('89), endeavoured to cut this Gordian knot by assuming that the character of each cell is determined by pangens that migrate from the nucleus into the cytoplasm, and, there becoming active, set up specific changes and determine the character of the cell, this way or that, according to their nature. But what influence guides the migrations of the pangens, and so correlates the operations of development? Both Driesch and Oscar Hertwig have attempted to answer this question, though the first-named author does not commit himself to the pangen-hypothesis. These writers have maintained that the particular mode of development in a given region or blastomere of the egg is *a result of its relation to the remainder of the mass, i.e.* a product of what may be called the intra-embryonic environ-

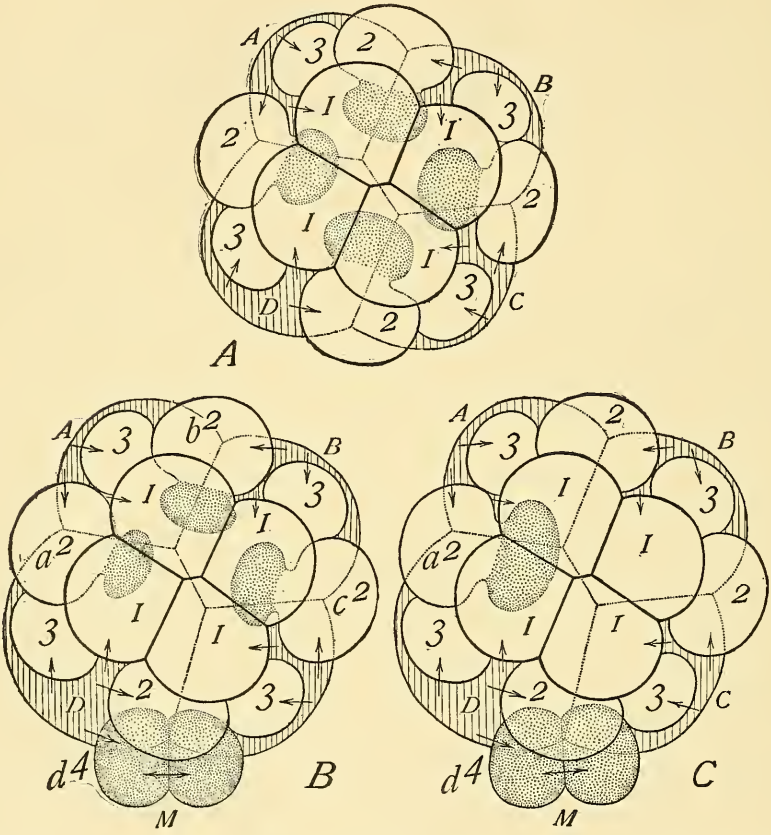

Fig. 188. — Diagrams illustrating the value of the quartets in a polyclade (*Leptoplana*), a lamellibranch (*Unio*), and a gasteropod (*Crepidula*). *A. Leptoplana*, showing mesoblast-formation in the second quartet. *B. Crepidula*, showing source of ectomesoblast (from a^2, b^2, c^2) and entomesoblast (from quadrant *D*). *C. Unio*, ectomesoblast formed only from a^2.

In all the figures the successive quartets are numbered with Arabic figures; ectoblast unshaded, mesoblest dotted, entoblast vertically lined.

ment. Hertwig insisted that the organism develops as a whole as the result of a physiological interaction of equivalent blastomeres, the transformation of each being due not to an inherent specific power of self-differentiation, as Roux's mosaic-theory assumed, but to the action upon it of the whole system of which it is a part. "According to my conception," said Hertwig, "each of the first two blastomeres contains the formative and differentiating forces not simply for the production of a half-body, but for the entire organism; the left blastomere develops into the left half of the body only because it is placed in relation to a right blastomere."[1] Again, in a later paper: "The egg is a specifically organized elementary organism that develops epigenetically by breaking up into cells and their subsequent differentiation. Since every elementary part (*i.e.* cell) arises through the division of the germ, or fertilized egg, it contains also the germ of the whole, but during the process of development it becomes ever more precisely differentiated and determined by the formation of cytoplasmic products according to its position with reference to the entire organism (blastula, gastrula, etc.)."[2]

An essentially similar view was advocated by the writer ('93, '94) nearly at the same time, and the same general conception was expressed with great clearness and precision by Driesch shortly after Hertwig: "The fragments (*i.e.* cells) produced by cleavage are completely equivalent or indifferent." "The blastomeres of the sea-urchin are to be regarded as forming a uniform material, and they may be thrown about, like balls in a pile, without in the least degree impairing thereby the normal power of development."[3] "*The relative position of a blastomere in the whole determines in general what develops from it; if its position be changed, it gives rise to something different;* in other words, *its prospective value is a function of its position.*"[4]

In this last aphorism the whole problem of development is brought to a focus. It is clearly not a solution of the problem, but only a highly suggestive restatement of it; for everything turns upon how the relation of the part to the whole is conceived. Very little consideration is required to show that this relation cannot be a merely geometrical or rudely mechanical one, for in the eggs of different animals blastomeres may almost exactly correspond in origin and relative position, yet differ widely in their relation to the resulting embryo. Thus we find that the cleavage of polyclades, annelids, and gasteropods (Fig. 188) shows a really wonderful agreement in form, yet the individual cells differ markedly in prospective value. In all of these forms three quartets of micromeres are successively formed according to exactly the same remarkable law of the alternation of the spirals;[1] and, in all, the posterior cell of a fourth quartet lies at the hinder end of the embryo in precisely the same geometrical relation to the remainder of the embryo; yet in the gasteropods and annelids this cell gives rise to the mesoblast-bands and their products, in the polyclade to a part of the archenteron, while important differences also exist in the value of the other quartets. The relation of the part to the whole is therefore of a highly subtle character, the prospective value of a blastomere depending not merely upon its geometrical position, but upon its relation to the whole complex inherited organization of which it forms a part. The apparently simple conclusion stated in Driesch's clever aphorism thus leads to further problems of the highest complexity. It should be here pointed out that Driesch does not accept Hertwig's theory of the interaction of blastomeres as such, but, like Whitman, Morgan, and others, has brought forward effective arguments against that too simple and mechanical conception. That theory is, in fact, merely Schwann's cell-composite theory of the organism applied to the developing embryo, and the general arguments against that theory find some of their strongest support in the facts of growth and development.[2] This has been forcibly urged by Whitman ('93), who almost simultaneously with the statements of Driesch and Hertwig, cited above, expressed the conviction that the morphogenic process cannot be conceived as merely the sum total or resultant of the individual cell-activities, but operates as a unit without respect to cell-boundaries, precisely as De Bary concludes in the case of growing plant-tissues (p. 393), and the nature of that process is due to the organization of the egg as a whole.

---

[1] '92, 1, p. 481.

[2] '93, p. 793. It should be pointed out that Roux himself in several papers expressly recognizes the fact that development cannot be regarded as a pure mosaic-work, and that besides the power of self-differentiation postulated by his hypothesis we must assume a "correlative differentiation" or differentiating interaction of parts in the embryo. *Cf.* Roux, '92, '93, 1.

[3] Studien IV., p. 25.

[4] Studien IV., p. 39. *Cf.* His, "Es muss die Wachsthumserregbarkeit des Eies eine Function des Raumes sein." ('74, p. 153.)

While recognizing fully the great value of the results attained during the past few years in the field of experimental and speculative embryology, we are constrained to admit that as far as the essence of the problem is concerned we have not gone very far beyond the conclusions stated above; for beyond the fact that the inherited organization is involved in that of the germ-cells we remain quite ignorant of its essential nature. This has been recognized by no one more clearly than by Driesch himself, to whose critical researches we owe so much in this field. At the climax of a recent elaborate analysis, the high interest of which is somewhat obscured by

[1] *Cf.* p. 368.

[2] *Cf.* pp. 388–394.

its too abstruse form, Driesch can only reiterate his former aphorism,[1] finally taking refuge in an avowed theory of vitalism which assumes the localization of morphogenic phenomena to be determined by "a wholly unknown principle of correlation,"[2] and forms a problem *sui generis*.[3] This conclusion recognizes the fact that the fundamental problem of development remains wholly unsolved, thus confirming from a new point of view a conclusion which it is only fair to point out has been reached by many others.

But while the fundamental nature of the morphogenic process thus remains unknown, we have learned some very interesting facts regarding the conditions under which it takes place, and which show that Driesch's aphorism loses its meaning unless carefully qualified. The experiments referred to at pages 353, 410, show that up to a certain stage of development the blastomeres of the early echinoderm, *Amphioxus* or medusa-embryo, are "totipotent" (Roux), or "equipotential" (Driesch), *i.e.* capable of producing any or all parts of the body. Even in these cases, however, we cannot accept the early conclusion of Pflüger ('83), applied by him to the frog's egg, and afterward accepted by Hertwig, that the material of the egg, or of the blastomeres into which it splits up, is absolutely "isotropic," *i.e.* consists of quite uniform indifferent material, devoid of preëstablished axes. Whitman and Morgan, and Driesch himself, showed that this cannot be the case in the echinoderm egg; for the ovum possesses a polarity predetermined before cleavage begins, as proved by the fact that at the fourth cleavage a group of small cells or micromeres always arises at a certain point, which may be precisely located before cleavage by reference to the eccentricity of the first cleavage-nucleus,[4] and which, as Morgan showed,[5] is indicated before the third, and sometimes before the second cleavage, by a migration of pigment away from the micromere-pole. These observers are thus led to the assumption of a primary polarity of the egg-protoplasm, to which Driesch, in the course of further analysis of the phenomena, is compelled to add the assumption of a secondary polarity at right angles to the first.[6] These polarities, inherent not only in the entire egg, but also in each of the blastomeres into which it divides, form the primary conditions under which the bilaterally symmetrical organism develops by epigenesis. To this extent, therefore, the material of the blastomeres, though "totipotent," shows a certain predetermination with respect to the adult body.

---

[1] '99, pp. 86–87.

[2] This phrase is cited by Driesch from an earlier work ('92, p. 596) as giving a correct though "unanalytical" statement of his view. It may be questioned whether many readers will regard as an improvement the "analytical" form it assumes in his last work.

[3] *l.c.*, p. 90.

[4] *Cf.* Fig. 103.

[5] '94, p. 142.

[6] See Driesch, '93, pp. 229, 241; '96, and '99, p. 44.

We now proceed to the consideration of experiments which show that in some animal eggs such predetermination may go much farther, so that the development does, in fact, show many of the features of a mosaic-work, as maintained by Roux. The best-determined of these cases is that of the ctenophore-egg, as shown by the work of Chun, Driesch, and Morgan ('95), and Fischel ('98). These observers have demonstrated that isolated blastomeres of the two-, four-, or eight-cell stage undergo a cleavage which, through the earliest stages, is exactly like that which it would have undergone if forming part of a com-

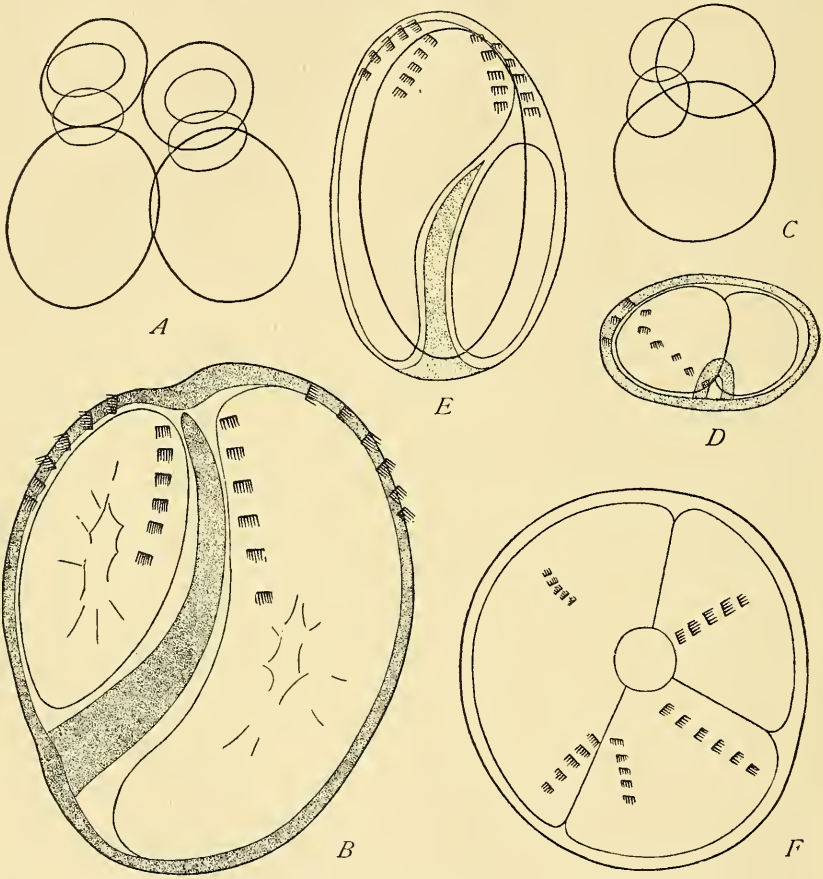

Fig. 189. — Partial larvæ of the ctenophore *Beroë*. [Driesch and Morgan.]

A. Half sixteen-cell stage, from an isolated blastomere. *B*. Resulting larva, with four rows of swimming-plates and three gastric pouches. *C*. One-fourth sixteen-cell stage, from an isolated blastomere. *D*. Resulting larva, with two rows of plates and two gastric pouches. *E*. Defective larva, with six rows of plates and three gastric pouches, from a nucleated fragment of an unsegmented egg. *F*. Similar larva with five rows of plates, from above.

plete embryo, and gives rise to a defective larva, having only four, two, or one row of swimming-plates (Fig. 189); and Fischel's observations give strong reason to believe that each of the eight micromeres of the sixteen-cell stage is definitely specified for the formation of one of the rows of plates. In like manner Crampton ('96) found that in case of the marine gasteropod *Ilyanassa* isolated blastomeres of two-cell or four-cell stages segmented exactly as if forming part of an entire embryo, and gave rise to *fragments* of a larva, not to complete dwarfs, as in the echinoderm (Fig. 190). Further, in embryos from which the "yolk-lobe" (a region of that macromere from which the primary mesoblast normally arises) had been removed, no mesoblast-bands were formed. Most interesting of all, Driesch and Morgan discovered that if a part of the cytoplasm of an *unsegmented* ctenophore-egg were removed, the remainder gave rise to an incomplete larva, showing definite defects (Fig. 189, *E*, *F*).

In none of these cases is the embryo able to complete itself, though it should be remarked that neither in the ctenophore nor in the snail is the partial embryo identical with a fragment of a whole embryo, since the micromeres finally enclose the macromeres, leaving no surface of fracture. This extreme is, however, connected by a series of forms with such cases as those of *Amphioxus* or the medusa, where the fragment develops nearly or quite as if it were a whole. In the tunicates the researches of Chabry ('87), Driesch ('94), and Crampton ('97) show that an isolated blastomere of the two-cell stage undergoes a typical half-cleavage (Crampton), but finally gives rise to a nearly perfect tadpole larva lacking only one of the asymmetrically placed sense-organs (Driesch). Next in the series may be placed the frog, where, as Roux, Endres, and Walter have shown, a blastomere of the two-cell stage may give rise to a typical half-morula, half-gastrula, and half-embryo[1] (Fig. 182), yet finally produces a perfect larva. A further stage is given by the echinoderm-egg, which, as Driesch showed, undergoes a half-cleavage and produces a half-blastula, which, however, closes to form a whole before the gastrula-stage (Fig. 183). Perfectly formed though dwarf larvæ result. Finally, we reach *Amphioxus* and the hydromasæ in which a perfect "whole development" usually takes place from the beginning, though it is a very interesting fact that the isolated blastomeres of *Amphioxus* sometimes show, in the early stages of cleavage, peculiarities of development that recall their behaviour when forming part of an entire embryo.[2]

We see throughout this series an effort, as it were, on the part of the isolated blastomere to assume the mode of development characteristic of a complete egg, but one that is striving against conditions that

---

[1] This is not invariably the case, as described beyond.

[2] *Cf.* Wilson, '93, pp. 590, 608.

tend to confine its operations to the *rôle* it would have played if still forming part of an entire developing egg. In *Amphioxus* or *Clytia* this tendency is successful almost from the beginning. In other forms the limiting conditions are only overcome at a later period, while in the ctenophore or snail they seem to afford an insurmountable barrier to complete development. What determines the limitations of development in these various cases? They cannot be due to nuclear specification; for in the ctenophore the fragment of an *unsegmented* egg, containing the normal egg-nucleus, gives rise to a defective larva; and my experiments on *Nereis* show that even in a highly

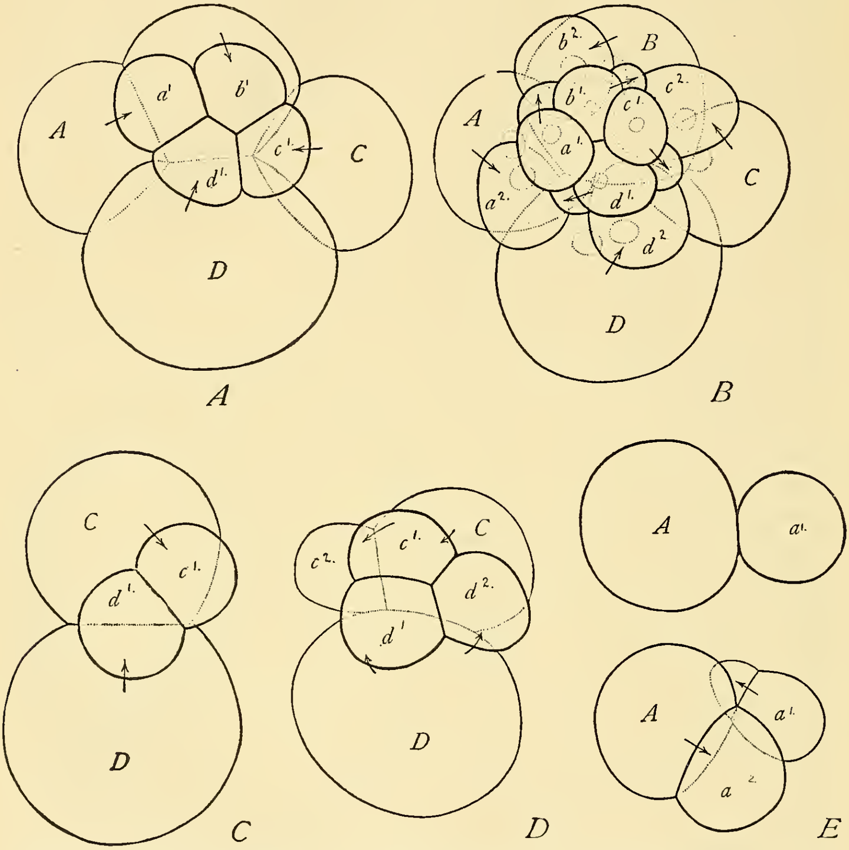

Fig. 190. — Partial development of isolated blastomeres of the gasteropod egg, *Ilyanassa*. [CRAMPTON.]

A. Normal eight-cell stage. *B.* Normal sixteen-cell stage. *C.* Half eight-cell stage, from isolated blastomere of the two-cell stage. *D.* Half twelve-cell stage succeeding. *E.* Two stages in the cleavage of an isolated blastomere of the four-cell stage; above a one-fourth eight-cell stage, below a one-fourth sixteen-cell stage.

determinate cleavage, essentially like that of the snail, the nuclei may be shifted about by pressure without altering the end-result. Neither can they lie in the form of the dividing mass as some authors have assumed; for in Crampton's experiments the half or quarter blastomere does not retain the form of a half or quarter sphere, but rounds

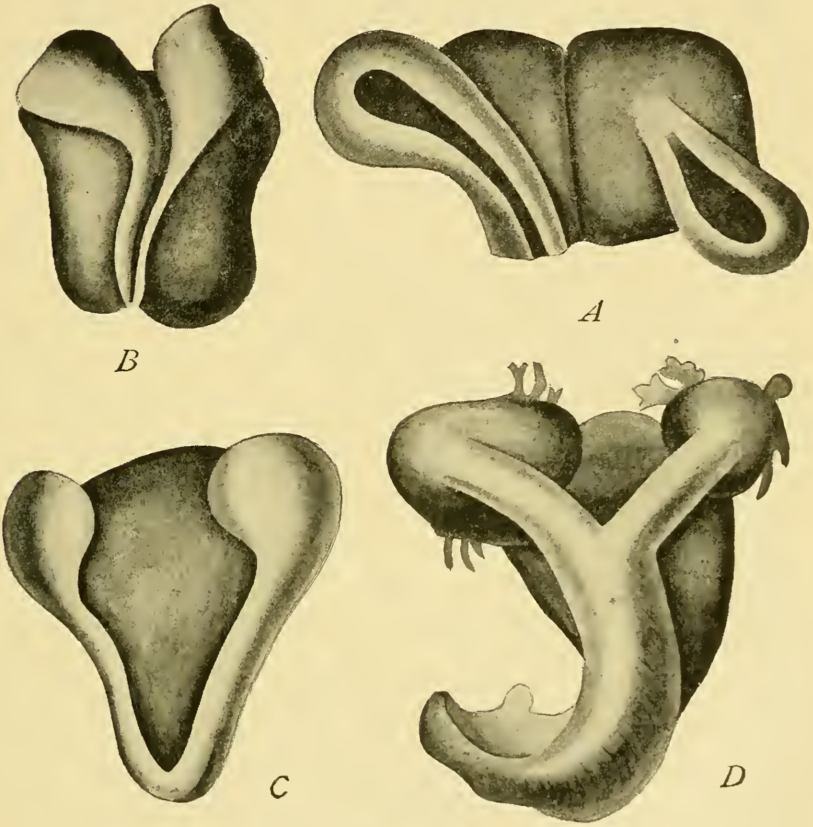

Fig. 191. — Double embryos of frog developed from eggs inverted when in the two-cell stage. [O. Schultze.]

A. Twins with heads turned in opposite directions. *B.* Twins united back to back. *C.* Twins united by their ventral sides. *D.* Double-headed tadpole.

off to a spheroid like the egg. But if the limiting conditions lie neither in the nucleus nor in the form of the mass, we must seek them in the *cytoplasm;* and if we find here factors by which the tendency of the part to develop into a whole may be, as it were, hemmed in, we shall reach a proximate explanation of the mosaic-like character of cleavage shown in the forms under consideration, and the mosaic theory of cytoplasmic localization will find a substantial if somewhat restricted basis.

That we are here approaching the true explanation is indicated by certain very remarkable and interesting experiments on the frog's egg, which prove that each of the first two blastomeres may give rise either to a half-embryo or to a whole embryo of half size, according to circumstances, and which indicate, furthermore, that these circumstances lie in a measure in the arrangement of the cytoplasmic materials. This most important result, which we owe especially to Morgan,[1] was reached in the following manner. Born had shown, in 1885, that if frogs' eggs be fastened in an abnormal position, — *e.g.* upside down, or on the side, — a rearrangement of the egg-material takes place, the heavier deutoplasm sinking toward the lower side, while the nucleus and protoplasm rise. *A new axis is thus established in the egg*, which has the same relation to the body-axes as in the ordinary development (though the pigment retains its original arrangement). This proves that in eggs of this character (telolecithal) the distribution of deutoplasm, or conversely of protoplasm, is one of the primary formative conditions of the cytoplasm; and the significant fact is that *by artificially changing this distribution the axis of the embryo is shifted.* Oscar Schultze ('94) discovered that if the egg be turned upside down when in the two-cell stage, a whole embryo (or half of a double embryo) may arise from each blastomere instead of a half-embryo as in the normal development, and that the axes of these embryos show no constant relation to one another (Fig. 191). Morgan ('95, 3) added the important discovery that either a half-embryo or a whole half-sized dwarf might be formed, *according to the position of the blastomere.* If, after destruction of one blastomere, the other be allowed to remain in its normal position, a half-embryo always results,[2] precisely as described by Roux. If, on the other hand, the blastomere be inverted, it may give rise either to a half-embryo[3] or to a whole dwarf.[4] Morgan therefore concluded that the production of whole embryos by the inverted blastomeres was, in part at least, due to a rearrangement or rotation of the egg-materials under the influence of gravity, the blastomere thus returning, as it were, to a state of equilibrium like that of an entire ovum.

This beautiful experiment gives most conclusive evidence that each of the two blastomeres contains all the materials, nuclear and cytoplasmic, necessary for the formation of a whole body; and that these materials may be used to build a whole body or half-body, according to the grouping that they assume. After the first cleavage takes place, each blastomere is *set*, as it were, for a half-development, but not so firmly that a rearrangement is excluded.

---

[1] *Anat. Anz.*, X. 19, 1895.

[2] Eleven cases observed.

[3] Three cases.

[4] Nine cases observed.

I have reached a nearly related result in the case of both *Amphioxus* and the echinoderms. In *Amphioxus* the isolated blastomere usually segments like an entire ovum of diminished size. This is, however, not invariable, for a certain number of such blastomeres show a more or less marked tendency to divide as if still forming part of an entire embryo. The sea-urchin *Toxopneustes* reverses this rule, for the isolated blastomere of the two-cell stage usually shows a perfectly typical half-cleavage, as described by Driesch, but in rare cases it may segment like an *entire* ovum of half-size (Fig. 183, *D*) and give rise to an entire blastula. We may interpret this to mean that in *Amphioxus* the differentiation of the cytoplasmic substance is at first very slight, or readily alterable, so that the isolated blastomere, as a rule, reverts at once to the condition of the entire ovum. In the sea-urchin, the initial differentiations are more extensive or more firmly established, so that only exceptionally can they be altered. In the snail and ctenophore we have the opposite extreme to *Amphioxus*, the cytoplasmic conditions having been so firmly established that they cannot be readjusted, and the development must, from the outset, proceed within the limits thus set up.

Through this conclusion we reconcile, as I believe, the theories of cytoplasmic localization and mosaic development with the hypothesis of cytoplasmic totipotence. Primarily the egg-cytoplasm is totipotent in the sense that its various regions stand in no fixed relation with the parts to which they respectively give rise, and the substance of each of the blastomeres into which it splits up contains all of the materials necessary to the formation of a complete body. Secondarily, however, development may assume more or less of a mosaic-like character through differentiations of the cytoplasmic substance involving local chemical and physical changes, deposits of metaplasmic material, and doubtless many other unknown subtler processes. Both the extent and the rate of such differentiations seem to vary in different cases; and here probably lies the explanation of the fact that the isolated blastomeres of different eggs vary so widely in their mode of development. When the initial differentiation is of small extent or is of such a kind as to be readily modified, cleavage is *indeterminate* in character and may easily be remodelled (as in *Amphioxus*). When they are more extensive or more rigid, cleavage assumes a mosaic-like or *determinate* character,[1] and qualitative division, in a certain sense, becomes a fact. Conklin's ('99) interesting observations on the highly determinate cleavage of gasteropods (*Crepidula*) show that here the substance of the attraction-spheres is unequally distributed, in a quite definite way, among the cleavage-cells, each sphere of a daughter-cell being carried over bodily into one of the granddaughter-cells (Fig. 192). We have here a substantial basis for the conclusion that in cleavage of this type qualitative division of the cytoplasm may occur.

---

[1] The convenient terms *indeterminate* and *determinate* cleavage were suggested by Conklin ('98).

It is important not to lose sight of the fact that development and differentiation do not in any proper sense first begin with the cleavage of the ovum, but long before this, during its ovarian history.[1] The primary differentiations thus established in the cytoplasm form the immediate conditions to which the later development must conform; and the difference between *Amphioxus* on the one hand, and the snail or ctenophore on the other, simply means, I think, that the initial differentiation is less extensive or less firmly established in the one than in the other.

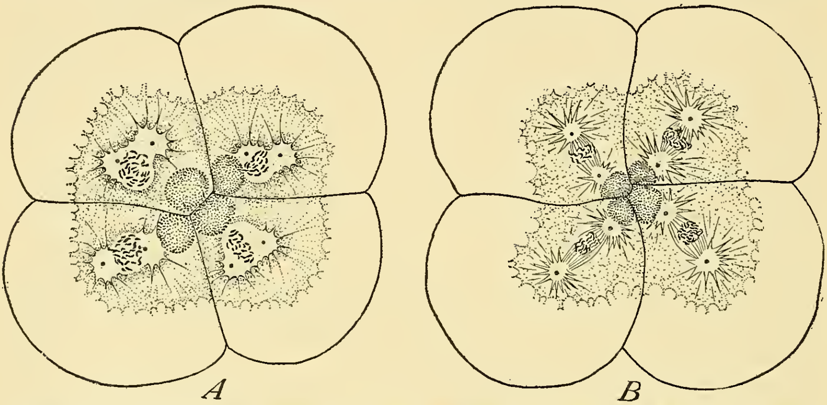

Fig. 192. — Two successive stages in the third cleavage of the egg of *Crepidula*, seen from the upper pole. [CONKLIN.]

In both figures the old spheres (dotted) lie at the upper pole of the embryo, and at the third cleavage they pass into the four respective cells of the first quartet of micromeres. The centrosomes are seen in the new spheres.

The origin of the cytoplasmic differentiations existing at the beginning of cleavage has already been considered (p. 386). If the conclusions there reached be placed beside the above, we reach the following conception. The primary determining cause of development lies in the nucleus, which operates by setting up a continuous series of specific metabolic changes in the cytoplasm. This process begins during ovarian growth, establishing the external form of the egg, its primary polarity, and the distribution of substances within it. The cytoplasmic differentiations thus set up form as it were a framework within which the subsequent operations take place in a course which is more or less firmly fixed in different cases. If the cytoplasmic conditions be artificially altered by isolation or other disturbance of the blastomeres, a readjustment may take place and development may be correspondingly altered. Whether such a readjustment is possible depends on secondary factors — the extent of the primary differentiations, the physical consistency of the egg-substance, the susceptibility of the protoplasm to injury, and doubtless a multitude of others. The same doubtless applies to the later stages of development; and we must here seek for some of the factors by which the power of regeneration in the adult is determined and limited. It is, however, not improbable, as pointed out below, that in the later stages differentiation may occur in the nuclear as well as in the cytoplasmic substance.

---

[1] See Wilson ('96), Driesch ('98, 1).

G. The Nucleus in Later Development

The foregoing conception, as far as it goes, gives at least an intelligible view of the more general features of early development and in a measure harmonizes the apparently conflicting results of experiment on various forms. But there are a very large number of facts relating especially to the later stages of differentiation, which it seems to leave unexplained, and which indicate that the nucleus as well as the cytoplasm may undergo progressive changes of its substance. It has been assumed by most critics of the Roux-Weismann theory that all of the nuclei of the body contain the same idioplasm, and that each therefore, in Hertwig's words, contains the germ of the whole. It is, however, doubtful whether this assumption is well founded. The power of a single cell to produce the entire body is in general limited to the earliest stages of cleavage, rapidly diminishes, and as a rule soon disappears entirely. When once the germ-layers have been definitely separated, they lose entirely the power to regenerate one another save in a few exceptional cases. In asexual reproduction, in the regeneration of lost parts, in the formation of morbid growths, each tissue is in general able to reproduce only a tissue of its own or a nearly related kind. Transplanted or transposed groups of cells (grafts and the like) retain more or less completely their autonomy and vary only within certain well-defined limits, despite their change of environment. All of these statements are, it is true, subject to exception; yet the facts afford an overwhelming demonstration that differentiated cells possess a specific character, that their power of development and adaptability to changed conditions becomes in a greater or less degree limited with the progress of development. As indicated above, this progressive specification of the tissue-cells is no doubt due in part to differentiation of the cytoplasm. There is, however, reason to suspect that, beyond this, *differentiation may sooner or later involve a specification of the nuclear substance.* When we reflect on the general *rôle* of the nucleus in metabolism and its significance as the especial seat of the formative power, we may well hesitate to deny that this part of Roux's conception may be better founded than his critics have admitted. Nägeli insisted that the idioplasm must undergo a progressive transformation during development, and many subsequent writers, including such acute thinkers as Boveri and Nussbaum, and many pathologists, have recognized the necessity for such an assumption. Boveri's remarkable observations on the nuclei of the primordial germ-cells in *Ascaris* demonstrate the truth of this view in a particular case; for here *all of the somatic nuclei lose a portion of their chromatin, and only the progenitors of the germ-neclei retain the entire ancestral heritage.* Boveri himself has in a measure pointed out the significance of his discovery, insisting that the specific development of the tissue-cells is conditioned by specific changes in the chromatin that they receive,[1] though he is careful not to commit himself to any definite theory. It hardly seems possible to doubt that in *Ascaris* the limitation of the somatic cells in respect to the power of development arises through a loss of particular portions of the chromatin. One cannot avoid the thought that further and more specific limitations in the various forms of somatic cells may arise through an analogous process, and that we have here a key to the origin of nuclear specification *without recourse to the theory of qualitative division.* We do not need to assume that the unused chromatin is cast out bodily; for it may degenerate and dissolve, or may be transformed into linin-substance or into nucleoli.

This suggestion is made only as a tentative hypothesis, but the phenomena of mitosis seem well worthy of consideration from this point of view. Its application to the facts of development becomes clearer when we consider the nature of the nuclear "control" of the cell, *i.e.* the action of the nucleus upon the cytoplasm. Strasburger, following in a measure the lines laid down by Nägeli, regards the action as essentially dynamic, *i.e.* as a propagation of molecular movements from nucleus to cytoplasm in a manner which might be compared to the transmission of a nervous impulse. When, however, we consider the *rôle* of the nucleus in synthetic metabolism, and the relation between this process and that of morphological synthesis, we must regard the question in another light; and opinion has of late strongly tended to the conclusion that nuclear "control" can only be explained as the result of active exchanges of material between nucleus and cytoplasm. De Vries, followed by Hertwig, assumes a migration of pangens from nucleus to cytoplasm, the character of the cell being determined by the nature of the migrating pangens, and these being, as it were, selected by circumstances (position of the cell, etc.). But, as already pointed out, the pangen-hypothesis should be held quite distinct from the purely physiological aspect of the question, and may be temporarily set aside; for specific nuclear substances may pass from the nucleus into the cytoplasm in an unorganized form. Sachs, followed by Loeb, has advanced the hypothesis that the development of particular organs is determined by specific "formative substances" which incite corresponding forms of metabolic activity, growth, and differentiation. It is but a step from this to the very interesting suggestion of Driesch that the nucleus is a storehouse of ferments which pass out into the cytoplasm and there set up specific activities. Under the influence of these ferments the cytoplasmic organization is determined at every step of the development, and new conditions are established for the ensuing change. This view is put forward only tentatively as a "fiction" or working hypothesis; but it is certainly full of suggestion. Could we establish the fact that the number of ferments or formative substances in the nucleus diminishes with the progress of differentiation, we should have a comparatively simple and intelligible explanation of the specification of nuclei and the limitation of development. The power of regeneration might then be conceived, somewhat as in the Roux-Weismann theory, as due to a retention of idioplasm or germ-plasm — *i.e.* chromatin — in a less highly modified condition, and the differences between the various tissues in this regard, or between related organisms, would find a natural explanation.

---

[1] '91, p. 433.

Development may thus be conceived as a progressive transformation of the egg-substance primarily incited by the nucleus, first manifesting itself by specific changes in the cytoplasm, but sooner or later involving in some measure the nuclear substance itself. This process, which one is tempted to compare to a complicated and progressive form of crystallization, begins with the youngest ovarian egg and proceeds continuously until the cycle of individual life has run its course. Cell-division is an accompaniment but not a direct cause of differentiation. The cell is no more than a particular area of the germinal substance comprising a certain quantity of cytoplasm and a mass of idioplasm in its nucleus. Its character is primarily a manifestation of the general formative energy acting at a particular point under given conditions. When once such a circumscribed area has been established, it may, however, emancipate itself in a greater or less degree from the remainder of the mass, and acquire a specific character so fixed as to be incapable of further change save within the limits imposed by its acquired character.

H. The External Conditions of Development

We have thus far considered only the internal conditions of development which are progressively created by the germ-cell itself. We must now briefly glance at the external conditions afforded by the environment of the embryo. That development is conditioned by the external environment is obvious. But we have only recently come to realize how intimate the rèlation is; and it has been especially the service of Loeb, Herbst, and Driesch to show how essential a part is played by the environment in the development of specific organic forms. The limits of this work will not admit of any adequate review of the vast array of known facts in this field, for which the reader is referred to the works especially of Herbst. I shall only consider one or two cases which may serve to bring out the general principle that they involve. Every living organism at every stage of its existence reacts to its environment by physiological and morphological changes. The developing embryo, like the adult, is a moving equilibrium — a product of the response of the inherited organization to the external stimuli working upon it. If these stimuli be altered, development is altered. This is beautifully shown by the experiments of Herbst and others on the development of sea-urchins. Pouchet and Chabry showed that if the embryos of these animals be made to develop in sea-water containing no lime-salts, the larva fails to develop not only its calcareous skeleton, but also its ciliated arms, and a larva thus results that resembles in some particulars an entirely different specific form; namely, the *Tornaria* larva of *Balanoglossus*. This result is not due simply to the lack of necessary material; for Herbst showed that the same result is attained if a slight excess of potassium chloride be added to sea-water containing the normal amount of lime (Fig. 193). In the latter case the specific metabolism of the protoplasm is altered by a particular chemical stimulus, and a new form results.

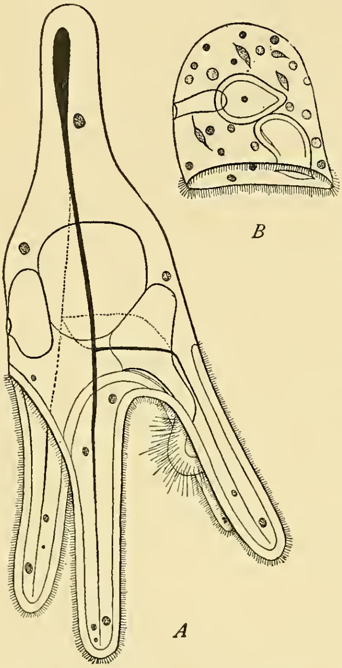

Fig. 193. — Normal and modified larvæ of sea-urchins. [Herbst.]

A. Normal Pluteus (*Strongylocentrotus*). *B.* Larva (*Sphærechinus*) at the same stage as the foregoing, developed in sea-water containing a slight excess of potassium chloride.

The changes thus caused by slight chemical alterations in the water may be still more profound. Herbst ('92) observed, for example, that when the water contains a very small percentage of lithium chloride, the blastula of sea-urchins fails to invaginate to form a typical gastrula, but *evaginates* to form an hour-glass-shaped larva, one half of which represents the archenteron, the other half the ectoblast. Moreover, a much larger number of the blastula-cells undergo the differentiation into entoblast than in the normal development, the ectoblast sometimes becoming greatly reduced and occasionally disappearing altogether, so that the entire blastula is

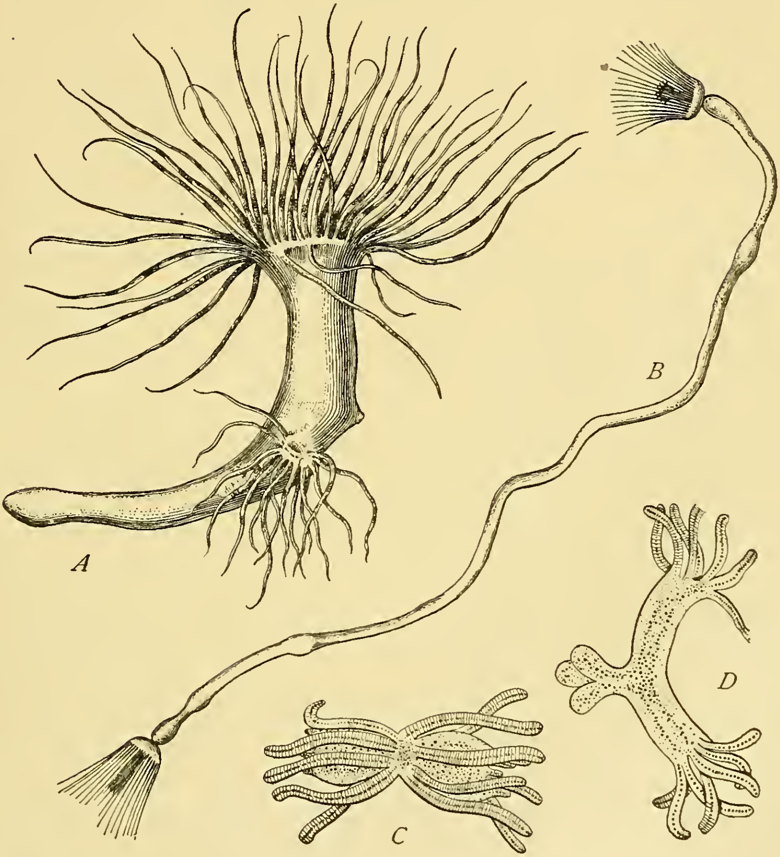

Fig. 194. — Regeneration in cœlenterates (*A*, *B*, from LOEB; *C*, *D*, from BICKFORD).

A. Polyp (*Cerianthus*), producing new tentacles from the *aboral* side of a lateral wound. *B*. Hydroid (*Tubularia*), generating a head at each end of a fragment of the stem suspended in water. *C*. *D*. Similar generation of heads at both ends of short pieces of the stem, in *Tubularia*.

differentiated into cells having the histological character of the normal entoblast! One of the most fundamental of embryonic differentiations is thus shown to be intimately conditioned by the chemical environment.

The observations of botanists on the production of roots and other structures as the result of local stimuli are familiar to all. Loeb's interesting experiments on hydroids give a similar result ('91). It has long been known that *Tubularia*, like many other hydroids, has the power to regenerate its "head" — *i.e.* hypostome, mouth, and tentacles — after decapitation. Loeb proved that in this case the power to form a new head is conditioned by the environment. For if a *Tubularia* stem be cut off at both ends and inserted in the sand upside down, *i.e.* with the oral end buried, a new head is regenerated at the free (formerly aboral) end. Moreover, if such a piece be suspended in the water by its middle point, a new head is produced at *each end* (Fig. 194); while if both ends be buried in the sand, neither end regenerates. This proves in the clearest manner that in this case the power to form a definite complicated structure is called forth by the stimulus of the external environment.

These cases must suffice for our purpose. They prove incontestably that *normal development is in a greater or less degree the response of the developing organism to normal conditions*; and they show that we cannot hope to solve the problems of development without reckoning with these conditions. But neither can we regard specific forms of development as *directly caused* by the external conditions; for the egg of a fish and that of a polyp develop, side by side, in the same drop of water, under identical conditions, each into its predestined form. Every step of development is a physiological reaction, involving a long and complex chain of cause and effect between the stimulus and the response. The character of the response is determined, not by the stimulus, but by the *inherited organization*. While, therefore, the study of the external conditions is essential to the analysis of embryological phenomena, it serves only to reveal the mode of action of the germ and gives but a dim insight into its ultimate nature.

I. Development, Inheritance, and Metabolism

In bringing the foregoing discussion into more direct relation with the general theory of cell-action, we may recall that the cell-nucleus appears to us in two apparently different *rôles*. On the one hand, it is a primary factor in morphological synthesis and hence in inheritance, on the other hand an organ of metabolism especially concerned with the constructive process. These two functions we may with

Claude Bernard regard as but different phases of one process. The building of a definite cell-product, such as a muscle-fibre, a nerve-process, a cilium, a pigment-granule, a zymogen-granule, is in the last analysis the result of a specific form of metabolic activity, as we may conclude from the fact that such products have not only a definite physical and morphological character, but also a definite chemical character. In its physiological aspect, therefore, inheritance is the recurrence, in successive generations, of like forms of metabolism; and this is effected through the transmission from generation to generation of a specific substance or idioplasm which we have seen reason to identify with chromatin. The validity of this conception is not affected by the form in which we conceive the morphological nature of the idioplasm — whether as simply a mixture of chemical substances, as a microcosm of invisible germs or pangens, as assumed by De Vries, Weismann, and Hertwig, as a storehouse of specific ferments as Driesch suggests, or as a complex molecular substance grouped in micellæ as in Nägeli's hypothesis. It is true, as Verworn insists, that the cytoplasm is essential to inheritance; for without a specifically organized cytoplasm the nucleus is unable to set up specific forms of synthesis. This objection, which has already been considered from different points of view, by both De Vries and Driesch, disappears as soon as we regard the egg-cytoplasm as *itself a product of the nuclear activity;* and it is just here that the general *rôle* of the nucleus in metabolism is of such vital importance to the theory of inheritance. If the nucleus be the formative centre of the cell, if nutritive substances be elaborated by or under the influence of the nucleus while they are built into the living fabric, then the specific character of the cytoplasm is determined by that of the nucleus, and the contradiction vanishes. In accepting this view we admit that the cytoplasm of the egg is, in a measure, the substratum of inheritance, but it is so only by virtue of its relation to the nucleus, which is, so to speak, the ultimate court of appeal. The nucleus cannot operate without a cytoplasmic field in which its peculiar powers may come into play; but this field is created and moulded by itself.

J. PREFORMATION AND EPIGENESIS. THE UNKNOWN FACTOR IN DEVELOPMENT

We have now arrived at the farthest outposts of cell-research, and here we find ourselves confronted with the same unsolved problems before which the investigators of evolution have made a halt. For we must now inquire what is the guiding principle of embryological development that correlates its complex phenomena and directs them to a definite end. However we conceive the special mechanism of development, we cannot escape the conclusion that the power behind it is involved in the structure of the germ-plasm inherited from foregoing generations. What is the nature of this structure and how has it been acquired? To the first of these questions we have as yet no certain answer. The second question is merely the general problem of evolution stated from the standpoint of the cell-theory. The first question raises once more the old puzzle of preformation or epigenesis. The pangen-hypothesis of De Vries and Weismann recognizes the fact that development is epigenetic in its external features; but like Darwin's hypothesis of pangenesis, it is at bottom a theory of preformation, and Weismann expresses the conviction that an epigenetic development is an impossibility.[1] He thus explicitly adopts the view, long since suggested by Huxley, that "the process which in its superficial aspect is epigenesis appears in essence to be evolution in the modified sense adopted in Bonnet's later writings; and development is merely the expansion of a potential organism or 'original preformation' according to fixed laws."[2] Hertwig ('92, 2), while accepting the pangen-hypothesis, endeavours to take a middle ground between preformation and epigenesis, by assuming that the pangens (idioblasts) represent only *cell-characters*, the traits of the multicellular body arising epigenetically by permutations and combinations of these characters. This conception certainly tends to simplify our ideas of development in its outward features, but it does not explain why cells of different characters should be combined in a definite manner, and hence does not reach the ultimate problem of inheritance.

What lies beyond our reach at present, as Driesch has very ably urged, is to explain the orderly rhythm of development — the coordinating power that guides development to its predestined end. We are logically compelled to refer this power to the inherent organization of the germ, but we neither know nor can we even conceive what that organization is. The theory of Roux and Weismann demands for the orderly distribution of the elements of the germ-plasm a prearranged system of forces of absolutely inconceivable complexity. Hertwig's and De Vries's theory, though apparently simpler, makes no less a demand; for how are we to conceive the power which guides the countless hosts of migrating pangens throughout all the long and complex events of development? The same difficulty confronts us under any theory we can frame. If with Herbert Spencer we assume the germ-plasm to be an aggregation of like units, molecular or supra-molecular, endowed with predetermined polarities which lead to their grouping in specific forms, we but throw the problem one stage farther back, and, as Weismann himself has pointed out,[1] substitute for one difficulty another of exactly the same kind.

---

[1] *Germ-plasm*, p. 14.

[2] *Evolution, Science, and Culture*, p. 296.

The truth is that an explanation of development is at present beyond our reach. The controversy between preformation and epigenesis has now arrived at a stage where it has little meaning apart from the general problem of physical causality. What we know is that a specific kind of living substance, derived from the parent, tends to run through a specific cycle of changes during which it transforms itself into a body like that of which it formed a part; and we are able to study with greater or less precision the mechanism by which that transformation is effected and the conditions under which it takes place. But despite all our theories we no more know how the organization of the germ-cell involves the properties of the adult body than we know how the properties of hydrogen and oxygen involve those of water. So long as the chemist and physicist are unable to solve so simple a problem of physical causality as this, the embryologist may well be content to reserve his judgment on a problem a hundred-fold more complex.

The second question, regarding the historical origin of the idioplasm, brings us to the side of the evolutionists. The idioplasm of every species has been derived, as we must believe, by the modification of a preëxisting idioplasm through variation, and the survival of the fittest. Whether these variations first arise in the idioplasm of the germ-cells, as Weismann maintains, or whether they may arise in the body-cells and then be reflected back upon the idioplasm, is a question to which the study of the cell has thus far given no certain answer. Whatever position we take on this question, the same difficulty is encountered; namely, the origin of that coördinated *fitness*, that power of active adjustment between internal and external relations, which, as so many eminent biological thinkers have insisted, overshadows every manifestation of life. The nature and origin of this power is the fundamental problem of biology. When, after removing the lens of the eye in the larval salamander, we see it restored in perfect and typical form by regeneration from the posterior layer of the iris,[2] we behold an adaptive response to changed conditions of which the organism can have had no antecedent experience either ontogenetic or phylogenetic, and one of so marvellous a character that we are made to realize, as by a flash of light, how far we still are from a solution of this problem. It may be true, as Schwann himself urged, that the adaptive power of living beings differs in degree only, not in kind, from that of unorganized bodies. It is true that we may trace in organic nature long and finely graduated series leading upward from the lower to the higher forms, and we must believe that the wonderful adaptive manifestations of the more complex forms have been derived from simpler conditions through the progressive operation of natural causes. But when all these admissions are made, and when the conserving action of natural selection is in the fullest degree recognized, we cannot close our eyes to two facts: first, that we are utterly ignorant of the manner in which the idioplasm of the germ-cell can so respond to the influence of the environment as to call forth an adaptive variation; and second, that the study of the cell has on the whole seemed to widen rather than to narrow the enormous gap that separates even the lowest forms of life from the inorganic world.

---

[1] *Germinal Selection*, January, 1896, p. 284.

[2] See Wolff, '95, and Müller, '96.

I am well aware that to many such a conclusion may appear reactionary or even to involve a renunciation of what has been regarded as the ultimate aim of biology. In reply to such a criticism I can only express my conviction that the magnitude of the problem of development, whether ontogenetic or phylogenetic, has been underestimated; and that the progress of science is retarded rather than advanced by a premature attack upon its ultimate problems. Yet the splendid achievements of cell-research in the past twenty years stand as the promise of its possibilities for the future, and we need set no limit to its advance. To Schleiden and Schwann the present standpoint of the cell-theory might well have seemed unattainable. We cannot foretell its future triumphs, nor can we doubt that the way has already been opened to better understanding of inheritance and development.

LITERATURE. IX

Barfurth, D. — Regeneration und Involution: *Merkel u. Bonnet*, *Ergeb.*, I.–VIII. 1891–99.

Boveri, Th. — Ein geschlechtlich erzeugter Organismus ohne mütterliche Eigenschaften: *Sitz.-Ber. d. Ges. f. Morph. und Phys. in München*, V. 1889. See also *Arch. f. Entw.* 1895.

Brooks, W. K. — The Law of Heredity. *Baltimore*, 1883.

Id. — The Foundations of Zoölogy. *New York*, 1899.

Davenport, C. B. — Experimental Morphology: I., II. *New York*, 1897, 1899.

Driesch, H. — Analytische Theorie der organischen Entwicklung. *Leipzig*, 1894.

Id. — Die Localisation morphogenetischer Vorgänge: *Arch. Entw.*, VII. 1. 1899.

Id. — Resultate und Probleme der Entwickelungs-physiologie der Tiere: *Merkel u. Bonnet*, *Ergeb.*, VIII., 1898. (Full literature.)

Herbst, C. — Über die Bedeutung der Reizphysiologie für die kausale Auffassung von Vorgängen in der tierischen Ontogenese: *Biol. Centralb.*, XIV., XV. 1894–95.

Hertwig, O. — Ältere und neuere Entwicklungs-theorien. *Berlin*, 1892.

Hertwig, O. — Urmund und Spina Bifida: *Arch. mik. Anat.*, XXXIX. 1892.

Id. — Über den Werth der Ersten Furchungszellen für die Organbildung des Embryo: *Arch. mik. Anat.*, XLII. 1893.

Id. — Zeit und Streitfragen der Biologie. I. *Berlin*, 1894. II. *Jena*, 1897.

Id. — Die Zelle und die Gewebe, II. *Jena*, 1898.

His, W. — Unsere Körperform und das physiologische Problem ihrer Entstehung. *Leipzig*, 1874.

Loeb, J. — Untersuchungen zur physiologischen Morphologie: I. Heteromorphosis. *Würzburg*, 1891. II. Organbildung und Wachsthum. *Würzburg*, 1892.

Id. — Some Facts and Principles of Physiological Morphology: *Wood's Holl Biol. Lectures.* 1893.

Morgan, T. H. — Experimental Studies of the Regeneration of Phanaria Maculata: *Arch. Entw.*, VII. 2, 3. 1898.

Id. — The Development of the Frog's Egg. *New York*, 1897.

Nägeli, C. — Mechanisch-physiologische Theorie der Abstammungslehre. *München u. Leipzig*, 1884.

Roux, W. — Über die Bedeutung der Kernteilungsfiguren. *Leipzig*, 1883.

Id. — Über das künstliche Hervorbringen halber Embryonen durch Zerstörung einer der beiden ersten Furchungskugeln, etc.: *Virchow's Archiv*, 114. 1888.

Id. — Für unsere Programme und seine Verwirklichung: *Arch. Entw.*, V. 2. 1897. (See also Gesammelte Abhandlungen über Entwicklungsmechanik der Organismen, 1895.)

Sachs, J. — Stoff und Form der Pflanzenorgane: *Ges. Abhandlungen*, II. 1893.

Weismann, A. — Essays upon Heredity, First Series. *Oxford*, 1891.

Id. — Essays upon Heredity, Second Series. *Oxford*, 1892.

Id. — Aussere Einflüsse als Entwicklungsreize. *Jena*, 1894.

Id. — The Germ-plasm. *New York*, 1893.

Whitman, C. O. — Evolution and Epigenesis: *Wood's Holl Biol. Lectures.* 1894.

Wilson, Edm. B. — On Cleavage and Mosaic-work: *Arch. für Entwicklungsm.*, III. 1. 1896. See also Literature, VIII., p. 394.)

GLOSSARY

[Obsolete terms are enclosed in brackets. The name and date refer to the first use of the word; subsequent changes of meaning are indicated in the definition.]

Achro′matin (see **Chromatin**), the non-staining substance of the nucleus, as opposed to chromatin; comprising the ground-substance and the linin-network. (Flemming, 1879.)

A′crosome (ἄκρον, apex, σῶμα, body), the apical body situated at the anterior end of head of spermatozoön. (Lenhossék, 1897.)

[**Akaryo′ta**] (see **Karyota**), non-nucleated cells. (Flemming, 1882.)

Ale′cithal (ἀ-priv.; λέκιθος, the yolk of an egg), having little or no yolk (applied to eggs). (Balfour, 1880.)

Alloplasma′tic (ἄλλος, different). Applied to active substances formed by differentiation from the protoplasm proper, *e.g.* the substance of cilia, of nerve-fibrillæ, and of muscle-fibrillæ. Alloplasmatic organs are opposed to "protoplasmatic," which arise only by division of preëxisting bodies of the same kind. (A. Meyer, 1896.)

Amito′sis (see **Mitosis**), direct or amitotic nuclear division; mass-division of the nuclear substance without the formation of chromosomes and amphiaster. (Flemming, 1882.)

Am′phiaster (ἀμφί, on both sides; ἀστήρ, a star), the achromatic figure formed in mitotic cell-division, consisting of two asters connected by a spindle. (Fol, 1877.)

Amphipy′renin (see **Pyrenin**), the substance of the nuclear membrane. (Schwarz, 1887.)

Amy′loplasts (ἄμυλον, starch; πλαστός, πλάσσειν, form), the colourless starch-forming plastids of plant-cells. (Errera, 1882.)

An′aphase (ἀνά, back or again), the later period of mitosis during the divergence of the daughter-chromosomes. (Strasburger, 1884.)

Aniso′tropy (see **Isotropy**), having a predetermined axis or axes (as applied to the egg). (Pflüger, 1883.)

Antherozo′ïd, the same as **Spermatozoïd**.

Anti′podal cone, the cone of astral rays opposite to the spindle-fibres. (Van Beneden, 1883.)

Archiam′phiaster (ἀρχι = first, + amphiaster), the amphiaster by which the first or second polar body is formed. (Whitman, 1878.)

Ar′choplasma or **Archoplasm** (ἄρχων, a ruler) (sometimes written *archiplasm*), the substance from which the attraction-sphere, the astral rays, and the spindle-fibres are developed, and of which they consist. (Boveri, 1888.)

Arrhe′noid (ἄρρην, male). The sperm-aster or attraction-sphere formed during the fertilization of the ovum. (Henking, 1890.)

As′ter (ἀστήρ, a star). 1. The star-shaped structure surrounding the centrosome. (Fol, 1877.) [2. The star-shaped group of chromosomes during mitosis (see **Karyaster**). (Flemming, 1892.)]

[**As′trocœle**] (ἀστήρ, a star; κοῖλος, hollow), a term somewhat vaguely applied to the space in which the centrosome lies. (Fol, 1891.)

As'trosphere (see **Centrosphere**). 1. The central mass of the aster, exclusive of the rays, in which the centrosome lies. Equivalent to the "attraction-sphere" of Van Beneden. (Fol, 1891; Strasburger, 1892.) 2. The entire aster exclusive of the centrosome. Equivalent to the "astral sphere" of Mark. (Boveri, 1895.)

Attraction-sphere (see **Centrosphere**), the central mass of the aster from which the rays proceed. Also the mass of "archoplasm," derived from the aster, by which the centrosome is surrounded in the resting cell. (Van Beneden, 1883.)

[**Au'toblast**] (*αὐτός*, self), applied by Altmann to bacteria and other minute organisms, conceived as independent solitary "bioblasts." (1890.)

Axial filament, the central filament, probably contractile, of the spermatozoön-flagellum. (Eimer, 1874.)

Basichro'matin (see **Chromatin**), the same as chromatin in the usual sense. That portion of the nuclear network stained by basic tar-colours. (Heidenhain, 1894.)

Bi'oblast (*βίος*, life; *βλαστός*, a germ), a term applied by Altmann to the hypothetical ultimate vital unit (equivalent to *plasome*), and identified by him as the "granulum."

Bi'ogen (*βίος*, life; -*γενής*, producing), equivalent to *plasome*, etc. (Verworn, 1895.)

Bi'ophores (*βίος*, life; -*φόρος*, bearing), the ultimate supra-molecular vital units. Equivalent to the *pangens* of De Vries, the *plasomes* of Wiesner, etc. (Weismann, 1893.)

Bi'oplasm (*βίος*, *πλάςμα*). The active "living, forming germinal material," as opposed to "formed material." Nearly equivalent to protoplasm in the wider sense. (Beale, 1870.)

Bi'oplast, equivalent to cell. (Beale, 1870.)

Bi'valent, applied to chromatin-rods representing two chromosomes joined end to end. (Häcker, 1892.)

Ble'pharoplast (*βλεφαρίς*, eye-lash or cilium). The centrosome-like bodies in plant-spermatids in connection with which the cilia of the spermatozoids are formed. (Webber, 1897.)

Cell-plate (see **Mid-body**), the equatorial thickening of the spindle-fibres from which the partition-wall arises during the division of plant-cells. (Strasburger, 1875.)

Cell-sap, the more liquid ground-substance of the nucleus. [Kölliker, 1865; more precisely defined by R. Hertwig, 1876.]

Central spindle, the primary spindle by which the centrosomes are connected, as opposed to the contractile mantle-fibres surrounding it. (Hermann, 1891.)

Cen'triole, a term applied by Boveri to a minute body or bodies ("Central-korn") within the centrosome. In some cases not to be distinguished from the centrosome. (Boveri, 1895.)

Centrodes'mus (*κέντρον*, centre; *δεςμός*, a band), the primary connection between the centrosomes, formed by a substance from which arises the central spindle. (Heidenhain, 1894.)

Centrodeu'toplasm, the granular material of the testis-cells which may contribute to the formation of the Nebenkern or to that of the idiozome. (Erlanger, 1897.)

Centrole'cithal (*κέντρον*, centre; *λέκιθος*, yolk), that type of ovum in which the deutoplasm is mainly accumulated in the centre. (Balfour, 1880.)

Cen'troplasm (*κέντρον*, centre; *πλάσμα*), the protoplasm forming the attraction-sphere or central region of the aster; the substance of the centrosphere. (Erlanger, 1895.)

Cen'trosome (κέντρον, centre; σῶμα, body), a body found at the centre of the aster or attraction-sphere, regarded by some observers as the active centre of cell-division and in this sense as the dynamic centre of the cell. Under its influence arise the asters and spindle (amphiaster) of the mitotic figure. (Boveri, 1888.)

Cen'trosphere, used in this work as equivalent to the "astrosphere" of Strasburger; the central mass of the aster from which the rays proceed and within which lies the centrosome. The attraction-sphere. [Strasburger, 1892; applied by him to the "astrosphere" and centrosome taken together.]

Chloroplas'tids (χλωρός, green; πλαστός, form), the green plastids or chlorophyll-bodies of plant and animal cells. (Schimper, 1883.)

Chro'matin (χρῶμα, colour), the deeply staining substance of the nuclear network and of the chromosomes, consisting of nuclein. (Flemming, 1879.)

Chro'matophore (χρῶμα, colour; -φόρος, bearing), a general term applied to the coloured plastids of plant and animal cells, including chloroplastids and chromoplastids. (Schaarschmidt, 1880; Schmitz, 1882.)

Chro'matoplasm (χρῶμα, colour; πλάσμα, anything formed or moulded), the substance of the chromoplastids and other plastids. (Strasburger, 1882.)

Chro'miole, the smallest chromatin-granules which by their aggregation form the larger chromomeres of which the chromosomes are composed. (Eisen, 1899.)

Chro'momere (χρῶμα, colour; μέρος, a part), one of the chromatin-granules of which the chromosomes are made up. Identified by Weismann as the "id." See **Chromiole**. (Fol, 1891.)

Chromoplas'tids (χρῶμα, colour; πλαστός, form), the coloured plastids or pigment-bodies other than the chloroplasts, in plant-cells. (Schimper, 1883.)

Chro'moplasts, net-knots or chromatin-nucleoli; also used by some authors as equivalent to **Chromoplastid**. (Eisen, 1899.)

Chro'mosomes (χρῶμα, colour; σῶμα, body), the deeply staining bodies into which the chromatic nuclear network resolves itself during mitotic cell-division. (Waldeyer, 1888.)

Cleavage-nucleus, the nucleus of the fertilized egg, resulting from the union of egg-nucleus and sperm-nucleus. (O. Hertwig, 1875.)

Cortical zone, the outer zone of the centrosphere. (Van Beneden, 1887.)

Cyano'philous (κύανος, blue; φιλεῖν, to love), having an especial affinity for blue or green dyes. (Auerbach.)

Cy'taster (κύτος, hollow (a cell); ἀστήρ, star), the same as **Aster**, 1. See **Karyaster.** (Flemming, 1882.)

[**Cy'toblast**] (κύτος, hollow (a cell); βλαστός, germ). 1. The cell-nucleus. (Schleiden, 1838.) 2. One of the hypothetical ultimate vital units (bioblasts or "granula") of which the cell is built up. (Altmann, 1890.) 3. A naked cell or "protoblast." (Kölliker.)

[**Cytoblaste'ma**] (see **Cytoblast**), the formative material from which cells were supposed to arise by "free cell-formation." (Schleiden, 1838.)

[**Cytochyle'ma**] (κύτος, hollow (a cell): χυλός juice), the ground-substance of the cytoplasm as opposed to that of the nucleus. (Strasburger, 1882.)

Cy'tode (κύτος, hollow (a cell); εἶδος, form), a non-nucleated cell. (Häckel, 1866.)

Cytodie'resis (κύτος, hollow (a cell); διαίρεσις, division), the same as **Mitosis.** (Henneguy, 1882.)

Cytohy'aloplasma (κύτος, hollow (a cell); ὕαλος, glass; πλάσμα, anything formed), the substance of the cytoreticulum in which are embedded the microsomes; opposed to nucleohyaloplasma. (Strasburger, 1882.)

Cy'tolymph (κύτος, hollow (a cell); *lympha*, clear water), the cytoplasmic ground-substance. (Häckel, 1891.)

Cytomi'crosomes (see **Microsome**), microsomes of the cytoplasm; opposed to nucleomicrosomes. (Strasburger, 1882.)

Cytomi'tome (κύτος, hollow (a cell); μίτωμα, from μίτος, thread), the cytoplasmic as opposed to the nuclear thread-work. (Flemming, 1882.)

Cy'toplasm (κύτος, πλάσμα). 1. The protoplasmic ground-substance as opposed to the granules. (Kölliker, 1863.) 2. Equivalent to protoplasm. (Kölliker, 1867.) 3. The substance of the cell-body as opposed to that of the nucleus. (Strasburger, 1882.)

Cytoretic'ulum, the same as **Cytomitome**. (Strasburger, 1882.)

Cy'tosome (κύτος, hollow (a cell); σῶμα, body). 1. The cell-body or cytoplasmic mass as opposed to the nucleus. (Häckel, 1891.) 2. A term used as parallel to chromosome to denote deeply staining definitely organized cytoplasmic filaments or other cytoplasmic structures composed of "cytochromatin." (Prenant, 1898.)

Der'matoplasm (δέρμα, skin), the living protoplasm asserted to form a part of the cell-membrane in plants. (Wiesner, 1886.)

Der'matosomes (δέρμα, skin; σῶμα, body), the plasomes which form the cell-membrane. (Wiesner, 1886.)

Determinant, a hypothetical unit formed as an aggregation of biophores, determining the development of a single cell or independently variable group of cells. (Weismann, 1891.)

[**Deuthy'alosome**] (δεύτ(ερος), second; see **Hyalosome**), the nucleus remaining in the egg after formation of the first polar body. (Van Beneden, 1883.)

Deu'toplasm (δεύτ(ερος), second; πλάσμα, anything formed), yolk, lifeless food-matters deposited in the cytoplasm of the egg; opposed to "protoplasm." (Van Beneden, 1870.)

Diakine'sis (διά, through), the segmented-spireme-stage, following the synapsis, in the primary oöcyte or spermatocyte, during which the chromosomes persist for a considerable period in the form of double rods. (Häcker, 1897.)

Directive bodies, the polar bodies. (Fr. Müller, 1848.)

Directive sphere, the attraction-sphere. (Guignard, 1891.)

Dispermy, the entrance of two spermatozoa into the egg.

Dispi'reme (see **Spireme**), that stage of mitosis in which each daughter-nucleus has given rise to a spireme. (Flemming, 1882.)

Dy'aster (δυάς, two; see **Aster**, 2), the double group of chromosomes during the anaphases of cell-division. (Flemming, 1882.)

Ectosphere (ἐκτός, outside), the outer or cortical zone of the attraction-sphere. (Ziegler, 1899.)

Egg-nucleus, the nucleus of the egg after formation of the polar bodies and before its union with the sperm-nucleus. Equivalent to the "female pronucleus" of Van Beneden. (O. Hertwig, 1875.)

Enchyle'ma (ἐν, in; χυλός, juice). 1. The more fluid portion of protoplasm, consisting of "hyaloplasma." (Hanstein, 1880.) 2. The ground-substance (cytolymph) of cytoplasm as opposed to the reticulum. (Carnoy, 1883.)

Endoplast, the cell-nucleus. (Huxley, 1853.)

Ener'gid, the cell-nucleus together with the cytoplasm lying within its sphere of influence. (Sachs, 1892.)

Entosphere, (ἐντός, inside), the inner or medullary zone of the attraction-sphere. (Ziegler, 1899.)

Equatorial plate, the group of chromosomes lying at the equator of the spindle during mitosis. (Van Beneden, 1875.)

Ergastic (ἐργάζομαι, to work). Applied to relatively passive substances "formed anew through activity of the protoplasm." Equivalent to metaplasmic. *Cf.* alloplasmatic. (A. Meyer, 1896.)

Ergastoplasm (ἐργάζομαι, to work). Nearly equivalent to the "kinoplasm" of Strasburger and the "ergoplasm" of Davidoff. The more active protoplasmic substance from which fibrillar formations arise. (Garnier, 1897.)

Ergoplasm (ἔργον, work). The active protoplasm of the egg (in tunicates), mainly derived from the achromatic part of the germinal vesicle, and giving rise in part or wholly to the polar spindle. Analogous to archoplasm and kinoplasm. (Davidoff, 1889.)

Erythro'philous (ἐρυθρός, red; φιγεῖν, to love), having an especial affinity for red dyes. (Auerbach.)

Ga'mete (γαμέτη, wife; γαμέτης, husband), one of two conjugating cells. Usually applied to the unicellular forms.

Gem'mule (see **Pangen**), one of the ultimate supra-molecular germs of the cell assumed by Darwin. (Darwin, 1868.)

[**Ge'noblasts**] (γένος, sex; βλαστός, germ), a term applied by Minot to the mature germ-cells. The female genoblast (egg or "thelyblast") unites with the male (spermatozoön or "arsenoblast") to form an hermaphrodite or indifferent cell. (Minot, 1877.)

Germinal spot, the nucleolus of the germinal vesicle. (Wagner, 1836.)

Germinal vesicle, the nucleus of the egg before formation of the polar bodies. (Purkinje, 1825.)

Germ-plasm, the same as idioplasm. (Weismann.)

Heterokine'sis (ἕτερος, different), qualitative nuclear division: a hypothetical mode of mitosis assumed to separate chromatins of different quality; opposed to homoökinesis or equation-division. (Weismann, 1892.)

Heterole'cithal (ἕτερος, different; λέκιθος, yolk), having unequally distributed deutoplasm (includes telolecithal and centrolecithal). (Mark, 1892.)

Heterotyp'ical mitosis (ἕτερος, different; see **Mitosis**), that mode of mitotic division in which the daughter-chromosomes remain united by their ends to form rings. (Flemming, 1887.)

[**Holoschi'sis**] (ὅλος, whole; σχίζειν, to split), direct nuclear division. Amitosis. (Flemming, 1882.)

Homole'cithal (ὁμός, the same, uniform; λέκιθος, yolk), equivalent to alecithal. Having little deutoplasm, equally distributed, or none. (Mark, 1892.)

Homoökine'sis or **Homæokine'sis** (ὁμός, the same), equation-division, separating equivalent chromatins; opposed to heterokinesis. (Weismann, 1892.)

Homœotyp'ical mitosis (ὅμοιος, like; see **Mitosis**), a form of mitosis occurring in the secondary spermatocytes of the salamander, differing from the usual type only in the shortness of the chromosomes and the irregular arrangement of the daughter-chromosomes. (Flemming, 1887.)

Hy'aloplasma (ὕαλος, glass; πλάσμα, anything formed). 1. The ground-substance of the cell as distinguished from the granules or microsomes. [Hanstein, 1880.] 2. The achromatic substance of the nucleus in which the chromatin-particles are embedded. (Strasburger, 1882.) 3. The ground-substance as distinguished from the reticulum or "spongioplasm." (Leydig, 1885.) 4. The exoplasm or peripheral protoplasmic zone in plant-cells. (Pfeffer.)

Hy'alosomes (ὕαλος, glass; σῶμα, body), nucleolar-like bodies but slightly stained by either nuclear or plasma stains. (Lukjanow, 1888.)

[**Hy'groplasma**] (ὑγρός, wet; πλάσμα, something formed), the more liquid part of protoplasm as opposed to the firmer stereoplasm. (Nägeli, 1884.)

Id, the hypothetical structural unit resulting from the successive aggregation of biophores and determinants. Identified by Weismann as the chromomere, or chromatin-granule. (Weismann, 1891.)

Idant, the hypothetical unit resulting from the successive aggregation of biophores, determinants, and Ids. Identified by Weismann as the chromosome. (Weismann, 1891.)

Id'ioblasts (ἴδιος, one's own; βλαστός, germ), the hypothetical ultimate units of the cell; the same as biophores. (O. Hertwig, 1893.)

Id'ioplasm (ἴδιος, one's own; πλάσμα, a thing formed), equivalent to the germ-plasm of Weismann. The substance, now generally identified with chromatin, which by its inherent organization involves the characteristics of the species. The physical basis of inheritance. (Nägeli, 1884.)

Id'iosome (ἴδιος, one's own; σῶμα, body), the same as idioblast or plasome. (Whitman, 1893.)

Idiozome (ἴδιος, specially formed; ζῶμα, girdle). The sphere, often called attraction-sphere and usually enclosing the centrosomes, found in the spermatids of animals. (Meves, 1897.)

Interfilar substance, the ground-substance of protoplasm as opposed to the thread-work. (Flemming, 1882.)

Interzonal fibres ("Filaments reunissants" of Van Beneden. "Verbindungsfasern" of Flemming and others). Those spindle-fibres that stretch between the two groups of daughter-chromosomes during the anaphase. Equivalent in some cases to the central spindle. (Mark, 1881.)

Iso'tropy (ἴσος, equal; τροπή, a turning), the absence of predetermined axes (as applied to the egg). (Pfluger, 1883.)

[**Ka'ryaster**] (κάρυον, nut, nucleus; see **Aster**, 2), the star-shaped group of chromosomes in mitosis. Opposed to cytaster. (Flemming, 1882.)

Karyenchy'ma (κάρυον, nut, nucleus; ἐν, in; χυμός, juice), the "nuclear sap." (Flemming, 1882.)

Karyokine'sis (κάρυον, nut, nucleus; κίνησις, change, movement), the same as mitosis. (Schleicher, 1878.)

[**Karyoly'ma**], the "karyolytic" (mitotic) figure. (Auerbach, 1876.)

Ka'ryolymph. The nuclear sap. (Häckel, 1891.)

[**Karyo'lysis**] (κάρυον, nut, nucleus; λύσις, dissolution), the supposed dissolution of the nucleus during cell-division. (Auerbach, 1874.)

[**Karyoly'tic figure**] (see **Karyolysis**), a term applied by Auerbach to the mitotic figure in living cells. Believed by him to result from the dissolution of the nucleus. (Auerbach, 1874.)

Karyomi'crosome (see **Microsome**), the same as nucleo-microsome.

Karyomi'tome (κάρυον, nut, nucleus; μίτωμα, from μίτος, a thread), the nuclear as opposed to the cytoplasmic thread-work. (Flemming, 1882.)

Karyomito'sis (κάρυον, nut, nucleus; see **Mitosis**), mitosis. (Flemming, 1882.)

Ka'ryon (κάρυον, nut, nucleus), the cell-nucleus. (Häckel, 1891.)

Ka'ryoplasm (κάρυον, nut, nucleus; πλάσμα, a thing formed), nucleoplasm. The nuclear as opposed to the cytoplasmic substance. (Flemming, 1882.)

Ka'ryosome (κάρυον, nut, nucleus; σῶμα, body). 1. Nucleoli of the "net-knot" type, staining with nuclear dyes, as opposed to plasmosomes or true nucleoli. (Ogata, 1883.) 2. The same as chromosome. (Platner, 1886.) 3. Caryosome. The cell-nucleus. (Watasé, 1894.)

[**Karyo'ta**] (κάρυον, nut, nucleus), nucleated cells. (Flemming, 1882.)

Karyothe'ca (κάρυον, nut, nucleus; θήκη, case, box), the nuclear membrane. (Häckel, 1891.)

Ki'noplasm (κινεῖν, to move; πλάσμα, a thing formed), nearly equivalent to archoplasm, but used in a broader sense to denote in general the more active elements of protoplasm from which arise fibrillæ, the substance of cilia, and (in plants) the peripheral "Hautschicht" from which the membrane is formed; opposed to the "trophoplasm" or nutritive plasm. (Strasburger, 1892.)

[**Lanthanin**] (*λανθάνειν*, to conceal), equivalent to oxychromatin. (Heidenhain, 1892.)

Leucoplas'tids (*λευκός*, white; *πλαστός*, form), the colourless plastids of plant-cells from which arise the starch-formers (amyloplastids), chloroplastids, and chromoplastids. (Schimper, 1883.)

Li'nin (**linum**, a linen thread), the substance of the "achromatic" nuclear reticulum. (Schwarz, 1887.)

Lininoplast, the true nucleolus or plasmosome. (Eisen, 1899.)

Macrocentrosome, a term applied to the "centrosome" in Boveri's sense, *i.e.* to the larger body in which lies the central granule. (Ziegler, 1898.) Probably synonymous with entosphere.

Maturation, the final stages in the development of the germ-cells. More specifically, the process by which the reduction of the number of chromosomes is effected.

Metakine'sis (see **Metaphase**) (*μετά*, beyond (*i.e.* further); *κίννησις*, movement), the middle stage of mitosis, when the chromosomes are grouped in the equatorial plate. (Flemming, 1882.)

Metanu'cleus, a term applied to the nucleolus after its extrusion from the germinal vesicle. (Häcker, 1892.)

Met'aphase, the middle stage of mitosis during which occurs the splitting of the chromosomes in the equatorial plate. (Strasburger, 1884.)

Met'aplasm (*μετά*, after, beyond; *πλάσμα*, a thing formed), a term collectively applied to the lifeless inclusions (deutoplasm, starch, etc.) in protoplasm as opposed to the living substance. (Hanstein, 1868.)

Micel'la, one of the ultimate supra-molecular units of the cell. (Nägeli, 1884.)

Microcentrosome, equivalent to the central granule or centriole of Boveri. (Ziegler, 1898.)

Microcen'trum, the centrosome or group of centrosomes united by a "primary centrodesmus," forming the centre of the astral system. (Heidenhain, 1894.)

Mi'cropyle (*μικρός*, small; *πύλη*, orifice), the aperture in the egg-membrane through which the spermatozoön enters. [First applied by Turpin, in 1806, to the opening through which the pollen-tube enters the ovule. *t.* Robert Brown.]

Mi'crosome (*μικρός*, small; *σῶμα*, body), the granules as opposed to the ground-substance of protoplasm. (Hanstein, 1880.)

Microsphere, the central region of the aster (centrosphere) at the centre of which lie the centrosomes. (Kostanecki and Siedlecki, 1896.)

Middle-piece, that portion of the spermatozoön lying behind the nucleus at the base of the flagellum. (Schweigger-Seidel, 1865.)

Mid-body ("Zwischenkörper"), a body or group of granules, probably comparable with the cell-plate in plants, formed in the equatorial region of the spindle during the anaphases of mitosis. (Flemming, 1890.)

Mi'tome (*μίτωμα*, from *μίτος*, a thread), the reticulum or thread-work as opposed to the ground-substance of protoplasm. (Flemming, 1882.)

[**Mitoschi'sis** (*μίτος*, thread; *σχίζειν*, to split), indirect nuclear division; mitosis. (Flemming, 1882.)

Mito'sis (*μίτος*, a thread), indirect nuclear division typically involving: *a*, the formation of an amphiaster; *b*, conversion of the chromatin into a thread (spireme); *c*, segmentation of the thread into chromosomes; *d*, splitting of the chromosomes. (Flemming, 1882.)

Mi'tosome (*μίτος*, a thread; *σῶμα*, body), a body derived from the spindle-fibres of the secondary spermatocytes, giving rise, according to Platner, to the middle-piece and the tail-envelope of the spermatozoön. Equivalent to the Nebenkern of La Valette St. George. (Platner, 1889.)

Nebenkern (**Paranucleus**), a name originally applied by Bütschli (1871) to an extranuclear body in the spermatid; afterwards shown by La Valette St. George and Platner to arise from the spindle-fibres of the secondary spermatocyte. Since applied to many forms of cytoplasmic bodies (yolk-nucleus, etc.) of the most diverse nature.

Nuclear plate. 1. The equatorial plate. (Strasburger, 1875.) 2. The partition-wall which sometimes divides the nucleus in amitosis.

Nuclein, the chemical basis of chromatin; a compound of nucleinic acid and albumin or albumin radicles. (Miescher, 1871.)

Nucleinic or **nucleic acid**, a complex organic acid, rich in phosphorus, and an essential constituent of chromatin.

Nucleo-albumin, a nuclein having a relatively high percentage of albumin. Distinguished from nucleo-proteids by containing paranucleinic acid which yields no xanthin-bodies.

[**Nucleochyle'ma**] (*χυλός*, juice), the ground-substance of the nucleus as opposed to that of the cytoplasm. (Strasburger, 1882.)

Nucleohy'aloplasma (see **Hyaloplasm**), the achromatic substance (linin) in which the chromatin-granules are suspended. (Strasburger, 1882.)

Nucleomi'crosomes (see **Microsome**), the nuclear (chromatin) granules as opposed to those of the cytoplasm. (Strasburger, 1882.)

Nu'cleoplasm. 1. The reticular substance of the (egg-) nucleus. (Van Beneden, 1875.) 2. The substance of the nucleus as opposed to that of the cell-body or cytoplasm. (Strasburger, 1882.)

Nucleo-pro'teid, a nuclein having a relatively high percentage of albumin. May be split into albumin and true nucleinic acid, the latter yielding xanthin-bodies.

Œde'matin (*οἴδημα*, a swelling), the granules or microsomes of the nuclear ground-substance. (Reinke, 1893.)

O'öcyte (**Ovocyte**) (*ᾠόν*, egg; *κύτος*, hollow (a cell)), the ultimate ovarian egg before formation of the polar bodies. The primary oöcyte divides to form the first polar body and the secondary oöcyte. The latter divides to form the second polar body and the mature egg. (Boveri, 1891.)

Oögen'esis, Ovogenesis (*ᾠόν*, egg; *γένεσις*, origin), the genesis of the egg after its origin by division from the mother-cell. Often used more specifically to denote the process of reduction in the female.

Oögo'nium, Ovogonium (*ᾠόν*, egg; *γονή*, generation). 1. The primordial mother-cell from which arises the egg and its follicle. (Pflüger.) 2. The descendants of the primordial germ-cell which ultimately give rise to the oöcytes or ovarian eggs. (Boveri, 1891.)

Oökine'sis (*ᾠόν*, egg; *κίνησις*, movement), the mitotic phenomena of the egg during maturation and fertilization. (Whitman, 1887.)

O'vocentre, the egg-centrosome during fertilization. (Fol, 1891.)

Oxychro'matin (*ὀξύς*, acid; see **Chromatin**), that portion of the nuclear substance stained by acid tar-colours. Equivalent to "linin" in the usual sense. (Heidenhain, 1894.)

Pangen'esis (*πᾶς* (*παν-*), all; *γένεσις*, production), the theory of gemmules, according to which hereditary traits are carried by invisible germs thrown off by the individual cells of the body. (Darwin, 1868.)

Pangens (*πᾶς* (*παν-*), all; *-γενής*, producing), the hypothetical ultimate supra-molecular units of the idioplasm, and of the cell generally. Equivalent to gemmules, micellæ, idioblasts, biophores, etc. (De Vries, 1889.)

Parachro'matin (see **Chromatin**), the achromatic nuclear substance (linin of Schwarz) from which the spindle-fibres arise. (Pfitzner, 1883.)

Parali'nin (see **Linin**), the nuclear ground-substance or nuclear sap. (Schwarz, 1887.)

Parami'tome (see **Mitome**), the ground-substance or interfilar substance of protoplasm, opposed to mitome. (Flemming, 1892.)

Paranu'clein (see **Nuclein**), the substance of true nucleoli or plasmosomes. Pyrenin of Schwarz. (O. Hertwig, 1878.) Applied by Kossel to "nucleins" derived from the cytoplasm. These are compounds of albumin and paranucleic acid which yields no xanthin-bodies.

Paranucleus (see **Nebenkern**).

Par'aplasm (παρά, beside; πλάσμα, something formed), the less active portion of the cell-substance. Originally applied by Kupffer to the cortical region of the cell (exoplasm), but now often applied to the ground-substance. (Kupffer, 1875.)

Per'iplast (περί, around; πλαστός, form). 1. The peripheral part of the cell, including those parts outside the nucleus or "endoplast." (Huxley, 1853.) 2. A term somewhat vaguely applied to the attraction-sphere. The term *daughter-periplast* is applied to the centrosome. (Vejdovský, 1888.)

Perisphere (περί, around), a term applied to the outer region of the attraction-sphere in nerve-cells, and opposed to an inner "centrosphere." (Lenhossék, 1895.)

Plasmocytes (πλάσμα, κύτος), colourless blood-corpuscles supposed to be free attraction-spheres. (Eisen, 1897.)

Plasmosphere, the same as **Perisphere**.

Plas'mosome (πλάσμα, something formed (*i.e.* protoplasmic); σῶμα, body), the true nucleus, distinguished by its affinity for acid tar-colours and other "plasma-stains." (Ogata, 1883.)

Pla'some (πλάσμα, a thing formed; σῶμα, body), the ultimate supra-molecular vital unit. See **Biophore, Pangen**. (Wiesner, 1890.)

Plas'tid (πλαςτός, form). 1. A cell, whether nucleated or non-nucleated. (Häckel, 1866.) 2. A general term applied to permanent cell-organs (chloroplasts, etc.) other than the nucleus and centrosome. (Schimper, 1883.)

Plas'tidule, the ultimate supra-molecular vital unit. (Elssberg, 1874; Häckel, 1876.)

Plas'tin, a term of vague meaning applied to a substance related to the nucleo-proteids and nucleo-albumins constituting the linin-network (Zacharias) and the cytoreticulum (Carnoy). (Reinke and Rodewald, 1881.)

Pluri'valent (*plus*, more; *valere*, to be worth), applied to chromatin-rods that have the value of more than one chromosome *sensu strictu*. (Häcker, 1892.)

Polar bodies (Polar globules), two minute cells segmented off from the ovum before union of the germ-nuclei. (Disc. by Carus, 1824; so named by Robin, 1862.)

Polar corpuscle, the centrosome. (Van Beneden, 1876.)

Polar rays (Polradien), a term sometimes applied to all of the astral rays as opposed to the spindle-fibres, sometimes to the group of astral rays opposite to the spindle-fibres.

Pole-plates (End-plates), the achromatic spheres or masses at the poles of the spindle in the mitosis of Protozoa, probably representing the attraction-spheres. (R. Hertwig, 1877.)

Polyspermy, the entrance into the ovum of more than one spermatozoön.

[**Prochro'matin**] (see **Chromatin**), the substance of true nucleoli, or plasmosomes. Equivalent to paranuclein of O. Hertwig. (Pfitzner, 1883.)

Pronuclei, the germ-nuclei during fertilization; *i.e.* the egg-nucleus (female pronucleus) after formation of the polar bodies, and the sperm-nucleus (male pronucleus) after entrance of the spermatozoön into the egg. (VAN BENEDEN, 1875.)

[**Prothy'alosome**] (see **Hyalosome**), an area in the germinal vesicle (of *Ascaris*) by which the germinal spot is surrounded, and which is concerned in formation of the first polar body. (VAN BENEDEN, 1883.)

Pro'toblast (πρῶτος, first; βλαστός, a germ). 1. A naked cell, devoid of a membrane. (KÖLLIKER.) 2. A blastomere of the segmenting egg which is the parent-cell of a definite part or organ. (WILSON, 1892.)

Pro'toplasm (πρῶτος, first; πλάσμα, a thing formed or moulded). The active or "living" cell-substance. By all earlier and some present writers applied only to the substance of the cell-body (equivalent to Strasburger's cytoplasm). By many later writers applied to the entire active substance of the cell (karyoplasm plus cytoplasm). (PURKINJE, 1840; H. VON MOHL, 1846.)

Pro'toplast (πρῶτος, first; πλάστος, formed). 1. The protoplasmic body of the cell, including nucleus and cytoplasm, regarded as a unit. Nearly equivalent to the energid of Sachs. (HANSTEIN; 1880.) 2. Used by some authors synonymously with plastid.

[**Pseudochro'matin**] (see **Chromatin**), the same as prochromatin. (PFITZNER, 1886.)

Pseudonu'clein (see **Nuclein**), the same as the paranuclein of Kossel. (HAMMARSTEN, 1894.)

Pseudo-reduction, the preliminary halving of the number of chromatin-rods as a prelude to the formation of the tetrads and to the actual reduction in the number of chromosomes in maturation. (RÜCKERT, 1894.)

Pyre'nin (πυρήν, the stone of a fruit; *i.e.* relating to the nucleus), the substance of true nucleoli. Equivalent to the paranuclein of Hertwig. (SCHWARZ, 1887.)

Pyre'noid (πυρήν, the stone of a fruit; like a nucleus), colourless plastids (leucoplastids), occurring in the chromatophores of lower plants, forming centres for the formation of starch. (SCHMITZ, 1883.)

Reduction, the halving of the number of chromosomes in the germ-nuclei during maturation.

Sarcode (σαρξ, flesh). The protoplasm of unicellular animals. (DU JARDIN, 1835.)

Sertoli-cells, the large, digitate, supporting, and nutritive cells of the mammalian testis to which the developing spermatozoa are attached. (Equivalent to "spermatoblast" as originally used by VON EBNER, 1871.)

Sper'matid (σπέρμα, seed), the final cells which are converted without further division into spermatozoa; they arise by division of the secondary spermatocytes or "Samenmütterzellen." (LA VALETE ST. GEORGE, 1886.)

Sper'matoblasts (σπέρμα, seed; βλαστός, germ), a word of vague meaning, originally applied to the supporting cell or Sertoli-cell, from which a group of spermatozoa was supposed to arise. By various later writers used synonymously with spermatid. (VON EBNER, 1871.)

Sper'matocyst (σπέρμα, seed; κύστις, bladder), originally applied to a group of sperm-producing cells ("spermatocytes"), arising by division from an "Ursamenzelle" or "spermatogonium." (LA VALETTE ST. GEORGE, 1876.)

Sper'matocyte (σπέρμα, seed; κύτος, hollow (a cell)), the cells arising from the spermatogonia. The *primary spermatocyte* arises by growth of one of the last generation of spermatogonia. By its division are formed two *secondary spermatocytes*, each of which gives rise to two spermatids (ultimately spermatozoa). (LA VALETTE ST. GEORGE, 1876.)

[Spermatogem'ma] (σπέρμα, seed; *gemma*, bud), nearly equivalent to spermatocyst. Differs in the absence of a surrounding membrane. [In mammals, La Valette St. Géorge, 1878.]

Spermatogen'esis (σπέρμα, seed; γένεσις, origin), the phenomena involved in the formation of the spermatozoön. Often used more specifically to denote the process of reduction in the male.

Spermatogo'nium ("Ursamenzelle") (σπέρμα, seed; γονή, generation), the descendants of the primordial germ-cells in the male. Each ultimate spermatogonium typically gives rise to four spermatozoa. (La Valette St. George, 1876.)

Spermatome'rites (σπέρμα, seed; μέρος, a part), the chromatin-granules into which the sperm-nucleus resolves itself after entrance of the spermatozoön. (In *Petromyzon*, Böhm, 1887.)

Sper'matosome (σπέρμα, seed; σῶμα, body), the same as spermatozoön. (La Valette St. George, 1878.)

Spermatozo'ïd (see **Spermatozoön**), the ciliated paternal germ-cells in plants. The word was first used by von Siebold as synonymous with spermatozoön.

Spermatozo'ön (σπέρμα, seed; ζῷον, animal), the paternal germ-cell of animals. (Leeuwenhoek, 1677.)

Sperm-nucleus, the nucleus of the spermatozoön; more especially applied to it after entrance into the egg before its union with the egg-nucleus. In this sense equivalent to the "male pronucleus" of Van Beneden. (O. Hertwig, 1875.)

Sper'mocentre, the sperm-centrosome during fertilization. (Fol, 1891.)

Spi'reme (σπείρημα, a thing wound or coiled; a skein), the skein or "Knäuel" stage of the nucleus in mitosis, during which the chromatin appears in the form of a thread, continuous or segmented. (Flemming, 1882.)

Spon'gioplasm (σπογγίον, a sponge; πλάσμα, a thing formed), the cytoreticulum. (Leydig, 1885.)

Ste'reoplasm (στερεός, solid), the more solid part of protoplasm as opposed to the more fluid "hygroplasm." (Nägeli, 1884.)

Substantia hyalina, the protoplasmic ground-substance or "hyaloplasm." (Leydig, 1885.)

Substantia opaca, the protoplasmic reticulum or "spongioplasm." (Leydig, 1885.)

Synap'sis (συνᾶπτω, to fuse together). A stage in the nucleus preceding the first maturation-division, characterized by the massing of the chromatin at one side of the nucleus. From it the chromatin-masses emerge in the reduced number. (Moore, 1895.)

Te'loblast (τέλος, end; βλαστός, a germ), large cells situated at the growing end of the embryo (in annelids, etc.), which bud forth rows of smaller cells. (Whitman, Wilson, 1887.)

Telole'cithal (τέλος, end; λέκιθος, yolk), that type of ovum in which the yolk is mainly accumulated in one hemisphere. (Balfour, 1880.)

Te'lophases, **Telokine'sis** (τέλος, end), the closing phases of mitosis, during which the daughter-nuclei are re-formed. (Heidenhain, 1894.)

To'noplasts (τόνος, tension; πλαστός, form), plastids from which arise the vacuoles in plant-cells. (De Vries, 1885.)

Trophoplasm (τροφή, nourishment; πλάσμα). 1. The nutritive or vegetative substance of the cell, as distinguished from the idioplasm. (Nägeli, 1884.) 2. The active substance of the cytoplasm other than the "kinoplasm" or archoplasm. (Strasburger, 1892.)

Tro'phoplasts (τροφή, nourishment; πλαστός, form), a general term, nearly equivalent to the "plastids" of Schimper, including "anaplasts" (amyloplasts), "autoplasts" (chloroplasts), and chromoplasts. (A. MEYER, 1882–83.)

Yolk-nucleus, a word of vague meaning applied to a cytoplasmic body, single or multiple, that appears in the ovarian egg. [Named "Dotterkern" by CARUS, 1850.)

Zy'gote or **Zy'gospore** (*ζυγόν*, a yoke), the cell produced by the fusion of two conjugating cells or gametes in some of the lower plants.

GENERAL LITERATURE-LIST

THE following list includes only the titles of works actually referred to in the text and those immediately related to them. For more complete bibliography the reader is referred to the literature-lists in the special works cited, especially the following. For reviews of the early history of the cell-theory see Remak's *Untersuchungen* ('50–'55), Huxley on the *Cell-theory* ('53), Sach's *History of Botany* and Tyson's *Cell-doctrine* ('78). An exhaustive review of the earlier literature on protoplasm, nucleus, and cell-division will be found in Flemming's *Zellsubstanz* ('82), and a later review of theories of protoplasmic structure in Bütschli's *Protoplasma* ('92) and in Fischer's *Fixierung, etc., des Protoplasmas* ('99). The earlier work on mitosis and fertilization is very thoroughly reviewed in Whitman's *Clepsine* ('78), Fol's *Hénogenie* ('79), and Mark's *Limax* ('81). For more recent general literature-lists see especially Hertwig's *Zelle und Gewebe* ('93, '98), Yves Delage ('95), Henneguy's *Cellule* ('96), Häcker's *Praxis und Theorie der Zellen und Befruchtungslehre* ('99), and the admirable reviews by Flemming, Boveri, Rückert, Meves, Roux, and others in Merkel and Bonnet's *Ergebnisse* ('91–'98).

The titles are arranged in alphabetical order, according to the system adopted in Minot's *Human Embryology*. Each author's name is followed by the date of publication (the first two digits being omitted, except in case of works published before the present century), and this by a single number to designate the paper, in case two or more works were published in the same year. For example, **Boveri, Th., '87, 2**, denotes the second paper published by Boveri in 1887.

In order to economize space, the following abbreviations are used for the journals most frequently referred to: —

ABBREVIATIONS

A. A.	Anatomischer Anzeiger.
A. B.	Archives de Biologie.
A. A. P.	Archiv für Anatomie und Physiologie.
A. m. A.	Archiv für mikroscopische Anatomie.
A. Entwm.	Archiv für Entwicklungsmechanik.
B. C.	Biologisches Centralblatt.
C. R.	Comptes Rendus.
J. M.	Journal of Morphology.
J. w. Bot.	Jahrbuch für wissenschaftliche Botanik.
J. Z.	Jenaische Zeitschrift.
M. A.	Müller's Archiv.
M. J.	Morphologisches Jahrbuch.
Q. J.	Quarterly Journal of Microscopical Science.
Z. A.	Zoologischer Anzeiger.
Z. w. Z.	Zeitschrift für wissenschaftliche Zoologie.

ALBRECHT, E., '98. Untersuchungen zur Structur des Seeigeleies: *Sitzb. Ges. Morph. Phys. München.*, 3. — **Altman, R., '86.** Studien über die Zelle, I.: *Leipzig.* — **Id., '87.** Die Genese der Zellen: *Leipzig.* — **Id., '89.** Über Nucleinsäure: *A. A. P.*, p. 524. — **Id., '90, '94.** Die Elementarorganismen und ihre Beziehung zu den Zellen: *Leipzig.* — **Amelung, E.**, '93. Über mittlere Zellgrösse: *Flora*, p. 176. — **Andrews, E. A.**, 98, 1. Filose Activities in Metazoan Eggs: *Zool. Bull.*, II., 1. — **Id.**, '98, 2. Activities of Polar Bodies of Cerebratulus: *Arch. Entwm.*, VI., 2. — **Andrews, G. F.**, '97. The Living Substance as Such and as Organism: *J. M.*, XII., 2, Suppl. — **Arnold, J.**, '79. Über feinere Struktur der Zellen, etc.: *Virchow's Arch.*, 1879. (See earlier papers.) — **Atkinson, G. F.**, '99. Studies on Reduction in Plants: *Bot. Gaz.*, XXVIII., 1, 2. — **Auerbach, L.**, '74. Organologische Studien: *Breslau.* — **Id.**, '91. Über einen sexuellen Gegensatz in der Chromatophilie der Keimsubstanzen: *Sitzungsber. der Königl. preuss. Akad. d. Wiss. Berlin*, XXXV. — **Id.** '96. Untersuchungen über die Spermatogenese von Paludina: *J. Z.*, XXX.

VON BAER, C. E., '28, '37. Über Entwickelungsgeschichte der Thiere. Beobachtung und Reflexion: I. *Königsberg*, 1828; II. 1837. — **Id.**, '34. Die Metamorphose des Eies der Batrachier: *Müller's Arch.* — **Balbiani, E. G.**, '61. Recherches sur les phénomènes sexuels des Infusoires: *Journ. de la Phys.*, IV. — **Id.**, '64. Sur la constitution du germe dans l'œuf animal avant la fécondation: *C. R.*, LVIII. — **Id.**, '76. Sur les phénomènes de la division du noyau cellulaire: *C. R.*, XXX., October, 1876. — **Id.**, '81. Sur la structure du noyau des cellules salivares chez les larves de Chironomus: *Z. A.*, 1881, Nos. 99, 100. — **Id.**, '89. Recherches expérimentales sur la merotomie des Infusoires ciliés: *Recueil Zool. Suisse*, January, 1889. — **Id.**, '91, 1. Sur les régénérations successives du peristome chez les Stentors et sur le rôle du noyau dans ce phénomène: *Z. A.*, 372, 373. — **Id.**, '91, 2. Sur la structure et division du noyau chez les Spirochona gemmipara: *Ann. d. Micrographie.* — **Id.**, '93. Centrosome et Dotterkern: *Journ. de l'anat. et de la physiol.*, XXIX. — **Balfour, F. M.**, '80. Comparative Embryology: I. 1880. — **Ballowitz**, '88–'91. Untersuchungen über die Struktur der Spermatozoen: 1. (birds) *A. m. A.*, XXXII., 1888; 2. (insects) *Z. w. Z.*, LX., 1890; 3. (fishes, amphibia, reptiles) *A. m. A.*, XXXVI., 1890; 4. (mammals) *Z. w. Z.*, 1891. — **Id.**, '89. Fibrilläre Struktur und Contractilität: *Arch. ges. Phys.*, XLVI. — **Id.**, '91, 2. Die innere Zusammensetzung des Spermatozoënkopfes der Säugetiere: *Centralb. f. Phys.*, V. — **Id.**, '95. Die Doppelspermatozoa der Dytisciden: *Z. w. Z.*, XLV., 3. — **Id.**, '97. Über Sichtbarkeit und Aussehen der ungefärbten Centrosomen in ruhenden Gewebszellen: *Z. w. Mic.* XIV. — **Id.**, '98. Zur Kenntniss der Zellsphäre: *Arch. Anat. Phys.*, '98, II., III. — **Van Bambeke, C.**, '93. Elimination d'éléments nucléaires dans l'œuf ovarien de Scorpæna scrofa: *A. B.*, XIII., 1. — **Id.**, '96. De l'emploi du terme Protoplasma: *Bull. Soc. Belge. Mic.*, XXII. — **Id.**, '97. À propos de la delimitation cellulaire: *Ibid.*, XXIII. — **Id.**, '98. Recherches sur l'oocyte de Pholcus phalangioides: *A. B.*, XV. — **De Bary**, '58. Die Conjugaten. — **Id.**, '62. Über den Bau und das Wesen der Zelle: *Flora*, 1862. — **Id.**, '64. Die Mycetozoa: 2d Ed., *Leipzig.* — **Barry, M.** Spermatozoa observed within the Mammiferous Ovum: *Phil. Trans.*, 1843. — **Beale, Lionel S.**, '61. On the Structure of Simple Tissues of the Human Body: *London.* — **Béchamp and Estor**, '82. De la constitution élémentaire des tissues: *Montpellier.* — **Belajeff, W.**, '89. Mittheilung über Bau und Entwicklung der Spermatozoiden: *Ber. D. Bot. Ges.* — **Id.**, '92, 1. Über den Bau und die Entwicklung der Antherozoiden, I., Characeen. — **Id.**, '92, 2. Über die Karyokinesis in den Pollenmutterzellen bei *Larix* und *Fritillaria*: *Sitzb. Warsch. Naturf. Ges.* — **Id.**, '94, 1. Zur Kenntniss der Karyokinese bei den Pflanzen: *Flora*, 1894, Ergänzungsheft. — **Id.**, '94, 2. Über Bau und Entwicklung der Spermatozoiden der Pflanzen: *Flora*, LIV. — **Id.**, '97, 1. Über den Nebenkern in Spermatogenen Zellen und die Spermatogenese bei den Farnkräuten: *Ber. D. Bot. Ges.*, XV. — **Id.**, '97, 2. Über die Spermatogenese bei den Schachtelhalmen: *Ibid.* — **Id.**, '97, 3. Über die Aehnlichkeit einiger Erscheinungen in der Spermatogenese bei Thieren und Pflanzen: *Ibid.* — **Id.**, '97, 4. Einige Streit-

fragen in den Untersuchungen über die Karyokinese: *Ibid.* — **Id., '98, 1.** Über die Reductionstheilung des Pflanzenkerns: *Ibid.*, XVI. — **Id., '98, 2.** Über die Cilienbildner in den spermatogenen Zellen: *Ibid.* — **Id., '99.** Über die Centrosomen in den spermatogenen Zellen: *Ibid.*, XVII., 6. — **Benda, C., '87.** Untersuchungen über den Bau des funktionirenden Samenkenkanälchens einiger Säugethiere: *A. m. A.* — **Id., '93.** Zellstrukturen und Zelltheilungen des Salamanderhodens: *Verh. d. Anat. Ges.*, 1893. — **Van Beneden, E., '70.** Recherches sur la composition et la signification de l'œuf: *Mém. cour. de l'Ac. roy. d. S. de Belgique*, 1870. — **Id., '75.** La maturation de l'œuf, la fécondation et les premières phases du développement embryonnaire des mammifères d'après des recherches faites chez le lapin: *Bull. Ac. roy. de Belgique*, XI. — **Id., '76, 1.** Recherches sur les Dicyémides: *Bull. Ac. roy. Belgique*, XLI., XLII. — **Id., '76, 2.** Contribution à l'histoire de la vésicule germinative et du premier noyau embryonnaire: *Ibid.*, XLI.; also *Q. J.*, XVI. — **Id., '83.** Recherches sur la maturation de l'œuf, la fécondation et la division cellulaire: *A. B.*, IV. — **Van Beneden and Julin, '84, 1.** La segmentation chez les Ascidiens et ses rapports avec l'organisation de la larve: *Ibid.*, V. — **Id., '84, 2.** La spermatogenèse chez l'Ascaride mégalocéphale: *Bull. Ac. roy. Belgique*, 3me ser., VII. — **Van Beneden, E., et Neyt, A., '87.** Nouvelles recherches sur la fécondation et la division mitosique chez l'Ascaride mégalocéphale: *Ibid.*, 1887. — **Bergh, R. S., '89.** Recherches sur les noyaux de l'Urostyla: *A. B.* IX. — **Id., '94.** Vorlesungen über die Zelle und die einfachen Gewebe: *Wiesbaden.* — **Id., '95.** Über die relativen Theilungspotenzen einiger Embryonalzellen: *A. Entm.*, II., 2. — **Bernard, Claude.** Leçons sur les Phénomènes de la Vie: 1st Ed. 1878, 2d Ed. 1885, *Paris.* — **Berthold, G., '86.** Studien über Protoplasma-mechanik: *Leipzig.* — **Bickford, E. E., '94.** Notes on Regeneration and Heteromorphosis of Tubularian Hydroids: *J. M.*, IX., 3. — **Biondi, D., '85.** Die Entwicklung der Spermatozoiden: *A. m. A.*, XXV. — **Blanc, H., '93.** Étude sur la fécondation de l'œuf de la truite: *Ber. Naturforsch. Ges. zu Freiburg*, VIII. — **Blochmann, F., '87, 2.** Über die Richtungskörper bei Insekteneiern: *M. J.*, XII. — **Id., '88.** Über die Richtungskörper bei unbefruchtet sich entwickelnden Insekteneiern: *Verh. naturh. med. Ver. Heidelberg*, N. F., IV., 2. — **Id., '89.** Über die Zahl der Richtungskörper bei befruchteten und unbefruchteten Bieneneiern: *M. J.* — **Id., '94.** Über die Kerntheilung bei Euglena: *B. C.*, XIV. — **Böhm, A., '88.** Über Reifung und Befruchtung des Eies von Petromyzon Planeri: *A. m. A.*, XXXII. — **Id., '91.** Die Befruchtung des Forelleneies: *Sitz.-Ber. d. Ges. f. Morph. u. Phys. München*, VII. — **Boll, Fr., '76.** Das Princip des Wachsthums: *Berlin.* — **Bonnet, C., 1762.** Considerations sur les Corps organisés: *Amsterdam.* — **Born, G., '85.** Über den Einfluss der Schwere auf das Froschei: *A. m. A.*, XXIV. — **Id., '94.** Die Structur des Keimbläschens im Ovarialei von Triton tæniatus: *A. m. A.*, XLIII. — **Bourne, G. C., '95.** A Criticism of the Cell-theory; being an Answer to Mr. Sedgwick's Article on the Inadequacy of the Cellular Theory of Development; *Q. J.*, XXXVIII., 1. — **Boveri, Th., '86.** Über die Bedeutung der Richtungskörper: *Sitz.-Ber. Ges. Morph. u. Phys. München*, II. — **Id., '87, 1.** Zellenstudien, Heft I.; *J. Z.*, XXI. — **Id., '87, 2.** Über die Befruchtung der Eier von *Ascaris megalocephala: Sitz.-Ber. Ges. Morph. Phys. München*, III. — **Id., '87, 2.** Über den Anteil des Spermatozoön an der Teilung des Eies: *Sitz.-Ber. Ges. Morph. Phys. München*, III., 3. — **Id., '87, 3.** Über Differenzierung der Zellkerne während der Furchung des Eies von Ascaris meg.: *A. A.*, 1887. — **Id., '88, 1.** Über partielle Befruchtung: *Sitz.-Ber. Ges. Morph. Phys. München*, IV., 2. — **Id., '88, 2.** Zellenstudien, II.: *J. Z.*, XXII. — **Id., '89.** Ein geschlechtlich erzeugter Organismus ohne mütterliche Eigenschaften: *Sitz.-Ber. Ges. Morph. Phys. München*, V. Trans. in *Am. Nat.*, March, '93. — **Id., '90.** Zellenstudien, Heft III.: *J. Z.*, XXIV. — **Id., '91.** Befruchtung: *Merkel und Bonnet's Ergebnisse*, I. — **Id.,**

'95, 1. Über die Befruchtungs- und Entwickelungsfähigkeit kernloser Seeigel-Eier, etc.: *A. Entwm.* II., 3.—**Id., '95, 2.** Über das Verhalten der Centrosomen bei der Befruchtung des Seeigeleies, nebst allgemeinen Bemerkungen über Centrosomen und Verwandtes: *Verh. d. Physikal.-med. Gesellschaft zu Würzburg,* N. F., XXIX., 1.—**Id., '96.** Zur Physiologie der Kern- und Zellteilung: *Sitzb. Phys.-Med. Ges. Würzburg.*—**Braem, F., '93.** Das Prinzip der organbildenden Keimbezirke und die entwicklungsmechanischen Studien von H. Driesch: *B. C.,* XIII., 4, 5.—**Brandt, H., '77.** Über Actinosphærium Eichhornii: *Dissertation, Halle,* 1877.—**Brass, A., '83–4.** Die Organisation der thierischen Zelle: *Halle.*—**Brauer, A., '92.** Das Ei von Branchipus Grubii von der Bildung bis zur Ablage: *Abh. preuss. Akad. Wiss.,* '92.—**Id., '93, 1.** Zur Kenntniss der Reifung des parthenogenetisch sich entwickelnden Eies von Artemia Salina: *A. m. A.,* XLIII.—**Id., '93, 2.** Zur Kenntniss der Spermatogenese von Ascaris megalocephala: *A. m. A.,* XLII.—**Id., '94.** Über die Encystierung von Actinosphærium Eichhornii: *Z. w. Z.,* LVIII., 2.—**Braus, '95.** Über Zellteilung und Wachstum des Tritoneies: *J. Z.,* XXIX.—**Brooks, W. K., '83.** The Law of Heredity: *Baltimore.* **Brown, H. H., '85.** On Spermatogenesis in the Rat: *Q. J.,* XXV.—**Brown, Robert, '33.** Observations on the Organs and Mode of Fecundation in Orchideæ and Asclepiadeæ: *Trans. Linn. Soc.,* 1833. **Brücke, C., '61.** Die Elementarorganismen: *Wiener Sitzber.,* XLIV., 1861. **Brunn, M. von, '89.** Beiträge zur Kenntniss der Samenkörper und ihrer Entwickelung bei Vögeln und Säugethieren: *A. m. A.,* XXXIII.—**De Bruyne, C., '95.** La sphère attractive dans les cellules fixes du tissu conjonctif: *Bull. Acad. Sc. de Belgique,* XXX.—**Bürger, O., '91.** Über Attractionssphären in den Zellkörpern einer Leibesflüssigkeit: *A. A.,* VI.—**Id., '92.** Was sind die Attractionssphären und ihre Centralkörper? *A. A.,* 1892.—**Bütschli, O., '73.** Beiträge zur Kenntniss der freilebenden Nematoden: *Nova acta acad. Car. Leopold,* XXXVI.—**Id., '75.** Vorläufige Mitteilungen über Untersuchungen betreffend die ersten Entwickelungsvorgänge im befruchteten Ei von Nematoden und Schnecken: *Z. w. Z.,* XXV.—**Id., '76.** Studien über die ersten Entwickelungsvorgänge der Eizelle, die Zellteilung und die Konjugation der Infusorien: *Abh. des Senckenb. Naturforscher-Ges.,* X.—**Id., '85.** Organisationsverhältnisse der Sog. Cilioflagellaten und der Noctiluca: *M. J.,* X.—**Id., '90.** Über den Bau der Bakterien, etc.: *Leipzig.*—**Id., '91.** Über die sogenannten Centralkörper der Zellen und ihre Bedeutung: *Verh. Naturhist. Med. Ver. Heidelberg,* 1891.—**Id., '92, 1.** Über die künstliche Nachahmung der Karyokinetischen Figuren: *Ibid.,* N. F., V.—**Id., '92, 2.** Untersuchungen über mikroskopische Schäume und das Protoplasma (full review of literature on protoplasmic structure): *Leipzig* (*Engelmann*).—**Id., '94.** Vorläufige Berichte über fortgesetzte Untersuchungen an Gerinnungsschäumen, etc.: *Verh. Naturhist. Ver. Heidelberg,* V.—**Id., '96.** Weitere Ausführungen über den Bau der Cyanophyceen und Bakterien: *Leipzig.*—**Id., '98.** Untersuchungen über Strukturen: *Leipzig* (*Engelmann*).

CALKINS, G. N., '95, 1. Observations on the Yolk-nucleus in the Eggs of Lumbricus: *Trans. N.Y. Acad. Sci.,* June, 1895.—**Id., '95, 2.** The Spermatogenesis of Lumbricus: *J. M.,* XI., 2.—**Id., '97.** Chromatin-reduction and Tetrad-formation in Pteridophytes: *Bull. Torrey Bot. Club,* XXIV.—**Id., '98, 1.** The Phylogenetic Significance of Certain Protozoan Nuclei: *Ann. N. Y. Acad. Sci.,* XI., 16.—**Id., '98, 2.** Mitosis in Noctiluca: Ginn & Co., Boston, also *J. M.,* XV., 3.—**Calberla, E., '78.** Der Befruchtungsvorgang beim Ei von Petromyzon Planeri: *Z. w. Z.,* XXX.—**Campbell, D. H., '88–9.** On the Development of Pilularia globulifera: *Ann. Bot.,* II.—**Carnoy, J. B., '84.** La biologie cellulaire: *Lierre.*—**Id., '85.** La cytodiérèse des Arthropodes: *La Cellule,* I.—**Id., '86.** La cytodiérèse de l'œuf: *La Cellule,* III.—**Id., '86.** La vésicule germinative et les globules

polaires chez quelques Nématodes: *La Cellule*, III. — **Id.**, **'86.** La segmentation de l'œuf chez les Nématodes: *La Cellule*, III., 1. — **Carnoy and Le Brun**, **'97, 1, '98, '99.** La vésicule germinative et les globules polaires chez les Batraciens: *La Cellule*, XII, XIV, XVI. — **Id.**, **'97, 2.** La fécondation chez l'Ascaris megalocephala: *La Cellule*, XIII. — **Castle, W. E.**, **'96.** The Early Embryology of Ciona intestinalis: *Bull. Mus. Comp. Zoöl.*, XXVII., 7. — **Chabry, L.**, **'87.** Contributions à l'embryologie normale et pathologique des ascidies simples: *Paris*, 1887. — **Child, C. M.**, **'97.** The Maturation and Fertilization of the Egg of Arenicola: *Trans. N. Y. Acad. Sci.*, XVI. — **Chittenden, R. H.**, **'94.** Some Recent Chemico-physiological Discussions regarding the Cell: *Am. Nat.*, XXVIII., Feb., 1894. — **Chun, C.**, **'90.** Über die Bedeutung der direkten Zelltheilung: *Sitzb. Schr. Physik.-Ökon. Ges. Königsberg*, 1890. — **Id.**, **'92, 1.** Die Dissogonie der Rippenquallen: *Festschr. f. Leuckart, Leipzig*, 1892. — **Id.**, **'92, 2.** (In Roux, '92, p. 55): *Verh. d. Anat. Ges.*, VI., 1892. — **Clapp, C. M.**, **'91.** Some Points in the Development of the Toad-Fish: *J. M.*, V. — **Clarke, J. Jackson**, **'95.** Observations on various Sporozoa: *Q. J.*, XXXVII., 3. — **Coe, W. R.**, **'99.** The Maturation and Fertilization of the Egg of Cerebratulus: *Zoöl. Jahrb.*, XII. — **Cohn, Ferd.**, **'51.** Nachträge zur Naturgeschichte des Protococcus pluvialis: *Nova Acta*, XXII. — **Conklin, E. G.**, **'94.** The Fertilization of the Ovum: *Biol. Lect., Marine Biol. Lab., Wood's Holl, Boston*, 1894. — **Id.**, **'96.** Cell-size and Body-size: *Rept. of Am. Morph. Soc. Science*, III., Jan. 10, 1896. — **Id.**, **'97, 1.** Nuclei and Cytoplasm in the Intestinal Cells of Land Isopods: *Am. Nat.*, Jan. — **Id.**, **'97, 2.** The Embryology of Crepidula: *J. M.*, XIII., 1. — **Id.**, **'98.** Cleavage and Differentiation: *Wood's Holl Biol. Lectures*. — **Id.**, **'99.** Protoplasmic Movement as a Factor in Differentiation: *Wood's Holl Biol. Lectures*. — **Crampton, H. E.**, **'94.** Reversal of Cleavage in a Sinistral Gasteropod: *Ann. N. Y. Acad. Sci.*, March, 1894. — **Id.**, **'97.** The Ascidian Half-Embryo: *Ibid.*, June 19. — **Id.**, **'99.** The Ovarian History of the Egg of Molgula: *J. M.*, XV., Suppl. — **Crampton and Wilson**, **'96.** Experimental Studies on Gasteropod Development (H. E. Crampton). Appendix on Cleavage and Mosaic-Work (E. B. Wilson): *A. Entwm.*, III., 1. — **Czermak, N.**, **'99.** Über die Desintegration und die Reintegration des Kernkörperchens, *etc.*: *A. A.*, XV., 22.

DARWIN, F., **'77.** On the Protrusion of Protoplasmic Filaments, *etc.*: *Q. J.* XVII. — **Davis, B. M.**, **'99.** The Spore-mother-cell of Anthoceros: *Bot. Gaz.*, XXVIII., 2. — **Debski, B.**, **'97.** Beobachtungen über Kerntheilung bei Chara: *J. w. B.*, XXX. — **Id.**, **'98.** Weitere Beobachtungen an Chara: *Ibid.*, XXXII., 4. — **Delage, Yves**, **'95.** La Structure du Protoplasma et les Théories sur l'hérédité et les grands Problèmes de la Biologie Générale: *Paris*, 1895. — **Id.**, **'98.** Embryons sans noyau maternel: *C. R.*, CXXVII., 15. — **Id.**, **'99.** La fécondation mérogonique et ses résultats: *C. R.*, Oct. 23. — **Demoor, J.**, **'95.** Contribution à l'étude de la physiologie de la cellule (indépendance fonctionelle du protoplasme et du noyau): *A. B.*, XIII. — **Dendy, A.**, **'88.** Studies on the Comparative Anatomy of Sponges: *Q. J.*, Dec., 1888. — **Dixon, H. H.**, **'94.** Fertilization of *Pinus*: *Ann. Bot.*, VIII. — **Id.**, **'96.** On the Chromosomes of Lilium longiflorum: *Proc. R. Ir. Ac.*, III. — **Doflein, F. J.**, **'97, 1.** Die Eibildung bei Tubularia: *Z. w. Z.*, LXII., 1. — **Id.**, **'97, 2.** Karyokinesis des Spermakerus: *A. m. A.*, L, 2. — **Dogiel, A. S.**, **'90.** Zur Frage über das Epithel der Harnblase: *A. m. A.*, XXXV. — **Driesch, H.**, **'92, 1.** Entwickelungsmechanisches: *A. A.*, VII., 18. — **Id.** Entwicklungsmechanische Studien, I., II., 1892, *Z. w. Z.*, LIII.; III.-VI., 1893, *Ibid.*, LV.; VII.-X., 1893: *Mitt. Zoöl. St. Neapel*, XI., 2. — **Id.**, **'94.** Analytische Theorie der organischen Entwicklung: *Leipzig*. — **Id.**, **'95, 1.** Von der Entwickelung einzelner Ascidienblastomeren: *A. Entwm.*, I., 3. — **Id.**, **'95, 2.** Zur Analysis der Potenzen embryonaler Organzellen: *Ibid.*, II. — **Id.**, **'98, 1.** Über den Organisation des

Eies: *Entwm.*, IV. — **Id.**, **'98, 2.** Von der Beendigung morphogener Elementarprocesse: *Arch. Entwm.*, VI. — **Id.**, **'98, 3.** Ueber rein-mütterliche Charaktere an Bastardlarven von Echiniden: *Ibid.*, VII., 1. — **Id.**, **'99.** Die Localisation morphogenetischer Vorgänge: *Ibid.*, VIII., 1. — **Driesch and Morgan, '95, 2.** Zur Analysis der ersten Entwickelungsstadien des Ctenophoreneies: *Ibid.*, II., 2. — **Drüner, L.**, **'94.** Zur Morphologie der Centralspindel: *J. Z.*, XXVIII. (XXI.). — **Id.**, **'95.** Studien über den Mechanismus der Zelltheilung: *Ibid.*, XXIX., 2. — **Düsing, C.**, **'84.** Die Regulierung des Geschlechtsverhältnisses: *Jena*, 1884.

VON EBNER, V., **'71.** Untersuchungen über den Bau der Samencanälchen und die Entwicklung der Spermatozoiden bei den Säugethieren und beim Menschen: *Inst. Phys. u. Hist. Graz.*, 1871 (*Leipzig*). — **Id.**, **'88.** Zur Spermatogenese bei den Säugethieren: *A. m. A.*, XXXI. — **Ehrlich, P.**, **'79.** Über die specifischen Granulationen des Blutes: *A. A. P.* (*Phys.*), 1879, p. 573. — **Eisen, G.**, **'97.** Plasmocytes: *Proc. Cal. Acad. Sci.*, I., 1. — **Id.**, **'99.** The Chromoplasts and the Chromioles: *B. C.*, XIX., 4. — **Eismond, J.**, **'95.** Einige Beiträge zur Kenntniss der Attraktionssphären und der Centrosomen: *A. A.*, X. — **Endres and Walter, '95.** Anstichversuche an Eiern von Rana fusca: *A. Entwm.*, II., 1. — **Engelmann, T. W.**, **'80.** Zur Anatomie und Physiologie der Flimmerzellen: *Arch. ges. Phys.*, XXIII. — **von Erlanger, R.**, **'96, 1.** — Die neuesten Ansichten über die Zelltheilung und ihre Mechanik: *Zoöl. Centralb.*, III., 2. — **Id.**, **'96, 2.** Zur Befruchtung des Ascariseies nebst Bemerkungen über die Struktur des Protoplasmas und des Centrosomas: *Z. A.*, XIX. — **Id.**, **'96, 3.** Neuere Ansichten über die Struktur des Protoplasmas: *Zoöl. Centralb.*, III., 8, 9. — **Id.**, **'96, 4.** Zur Kenntniss des feineren Baues des Regenwurmhodens, etc.: *A. m. A.*, XLVII. — **Id.**, **'96, 5.** Die Versonische Zelle: *Zoöl. Centralb.*, III., 3. — **Id.**, **'96, 6.** Die Entwicklung der männlichen Geschechtszellen: *Ibid.*, III., 12. — **Id.**, **'97, 1.** Über Spindelreste und den echten Nebenkern, etc.: *Zoöl. Centralb.*, IV., 1. — **Id.**, **'97, 2.** Über die sogenannte Sphäre in den männlichen Geschlechtszellen: *Ibid.*, IV., 5. — **Id.**, **'97, 3.** Über die Chromatinreduktion in der Entwicklung der männlichen Geschlechtszellen: *Ibid.*, IV., 8. — **Id.**, **'97, 4.** Beiträge zur Kenntniss des Protoplasmas, etc. *A. m. A.*, XLIX. — **Id.**, **'97, 5.** Über die Spindelbildung in den Zellen der Cephalopoden Keimscheibe: *B. C.*, XVII., 20. — **Id.**, **'98.** Über die Befruchtung, etc., des Seeigeleies: *B. C.*, XVIII., 1. — **Errera, '86.** Eine fundamentale Gleichgewichtsbedingung organischen Zellen: *Ber. Deutsch. Bot. Ges.*, 1886. — **Id.**, **'87.** Zellformen und Seifenblasen: *Tagebl. der 60 Versammlung deutscher Naturforscher und Aerzte zu Wiesbaden*, 1887.

FAIRCHILD, D. G., **'97.** Über Kerntheilung und Befruchtung bei Basidiobolus: *Jahrb. wiss. Bot.*, XXX. — **Farmer, J. B.**, **'93.** On nuclear division of the pollen-mother-cell of Lilium Martagon: *Ann. Bot.* VII., 27. — **Id.**, **'94.** Studies in Hepaticæ: *Ibid.*, VIII., 29. — **Id.**, **'95, 1.** Über Kernteilung in Lilium-Antheren, besonders in Bezug auf die Centrosomenfrage: *Flora*, 1895, p. 57. — **Id.**, **95, 2.** On Spore-formation and Nuclear Division in the Hepaticæ: *Ann. Bot.*, IX. — **Farmer and Moore, '95.** On the essential similarities existing between the heterotype nuclear divisions in animals and plants: *A. A.*, XI., 3. — **Farmer and Williams, '96.** On Fertilization, etc., in Fucus: *Ann. Bot.*, X. — **Fick, R.**, **'93.** Über die Reifung und Befruchtung des Axolotleies: *Z. w. Z.*, LVI., 4. — **Id.**, **'97.** Bemerkungen zu M. Heidenhain's Spannungsgesetz: *Arch. Anat. u. Phys.* (Anat.). — **Fiedler, C.**, **'91.** Entwickelungsmechanische Studien an Echinodermeneiern: *Festschr. Nägeli u. Kölliker*, Zurich, 1891. — **Field, G. W.**, **'95.** On the Morphology and Physiology of the Echinoderm Spermatozoön: *J. M.*, XI. — **Fischer, A.**, **'94, 1.** Zur Kritik der Fixierungsmethoden der Granula: *A. A.*, IX., 22. —

Id., **94, 2.** — Über die Geisseln einiger Flagellaten: *J. w. B.* XXVII. — **Id.**, **'95.** Neue Beiträge zur Kritik der Fixierungsmethoden: *A. A.*, X. — **Id.**, **'97.** Untersuchungen über den Bau der Cyanophyceen und Bakterien: *Jena, Fischer.* — **Id.**, **'99.** Fixierung, Färbung und Bau des Protoplasmas: *Ibid.* — **Flemming, W.**, **'75.** Studien in der Entwicklungsgeschichte der Najaden: *Sitzb. d. k. k. Akad. Wiss. Wien*, LXXI., 3. — **Id.**, **'79, 1.** Beiträge zur Kenntniss der Zelle und ihre Lebenserscheinungen, I.: *A. m. A.*, XVI. — **Id.**, **'79, 2.** Über das Verhalten des Kerns bei der Zelltheilung, etc.: *Virchow's Arch.*, LXXVII. — **Id.**, **'80.** Beiträge zur Kenntniss der Zelle und ihrer Lebenserscheinungen, II.: *A. m. A.*, XIX. — **Id.**, **'81.** Beiträge zur Kenntniss der Zelle und ihrer Lebenserscheinungen, III.: *Ibid.*, XX. — **Id.**, **'82.** Zellsubstanz, Kern und Zellteilung: *Leipzig*, 1882. — **Id.**, **'87.** Neue Beiträge zur Kenntniss der Zelle: *A. m. A.*, XXIX. — **Id.**, **'88.** Weitere Beobachtungen über die Entwickelung der Spermatosomen bei Salamandra maculosa: *Ibid.*, XXXI. — **Id.**, **'91–'97.** Zelle, I.–VI.: *Ergebn. Anat. u. Entwicklungsgesch.* (*Merkel and Bonnet*), 1891–'97. — **Id.**, **'91, 1.** Attraktionssphären u. Centralkörper in Gewebs- u. Wanderzellen: *A. A.* — **Id.**, **'91, 2.** Neue Beiträge zur Kenntniss der Zelle, II. Teil: *A. m. A.*, XXXVII. — **Id.**, **'95, 1.** Über die Struktur der Spinalganglienzellen: *Verhandl. der anat. Gesellschaft in Basel.* 17 April, 1895, p. 19. — **Id.**, **'95, 2.** Zur Mechanik der Zelltheilung: *A. m. A.*, XLVI. — **Id.**, **'97, 2.** Ueber den Bau der Bindegewebszellen, etc.: *Zeit. Biol.*, XXXIV. — **Floderus, M.**, **'96.** Über die Bildung der Follikelhüllen bei den Ascidien: *Z. w. Z.*, LXI., 2. — **Fol, H.**, **'73.** Die erste Entwickelung des Geryonideies: *J. Z.*, VII. — **Id.**, **'75.** Études sur le développement des Mollusques. — **Id.**, **'77.** Sur le commencement de l'hénogenie chez divers animaux: *Arch. Sci. Nat. et Phys. Genève*, LVIII. See also *Arch. Zoöl. Exp.*, VI. — **Id.**, **'79.** Recherches sur la fécondation et la commencement de l'hénogenie: *Mém. de la Soc. de physique et d'hist. nat., Genève.* XXVI. — **Id.**, **'91.** Le Quadrille des Centres. Un episode nouveau dans l'histoire de la fécondation: *Arch. des sci. phys. et nat.*, 15 *Avril*, 1891; also, *A. A.*, 9–10, 1891. — **Foot, K.**, **'94.** Preliminary Note on the Maturation and Fertilization of Allolobophora: *J. M.*, IX., 3, '94. — **Id.**, **'96.** Yolk-nucleus and Polar Rings: *Ibid.*, XII., 1. — **Id.**, **'97.** The Origin of the Cleavage Centrosomes: *J. M.*, XII., 3. — **Francotte, P.**, **'97.** Recherches sur la maturation, *etc.*, chez les Polyclades: *Mem. cour. Acad. Sci. Belg.* — **Frenzel, J.**, **'93.** Die Mitteldarmdrüse des Flusskrebses und die amitotische Zelltheilung: *A. m. A.*, XLI. — **Fromman, C.**, **'65.** Über die Struktur der Bindesubstanzzellen des Rückenmarks: *Centrl. f. med. Wiss.*, III., 6. — **Id.**, **'75.** Zur Lehre von der Structur der Zellen: *J. Z.*, IX. (earlier papers cited). — **Id.**, **'84.** Untersuchungen über Struktur, Lebenserscheinungen und Reactionen thierischer und pflanzlicher Zellen: *J. Z.*, XVII. — **Fürst, E.**, **'98.** Über Centrosomen bei Ascaris: *A. m. A.*, LII. — **Fulmer, E. L.**, **'98.** Cell-division in Pine Seedlings: *Bot. Gaz.*, XXVI., 4.

GALEOTTI, GINO, **'93.** Über experimentelle Erzeugung von Unregelmässigkeiten des karyokinetischen Processes: *Bei. zur patholog. Anat. u. z. Allg. Pathol.*, XIV., 2, *Jena*, *Fischer*, 1893. — **Gallardo, Angel**, **'96.** La Carioquinesis: *Ann. Soc. Cientif. Argentina*, XLII. — **Id.**, **'97.** Significado Dinamico de las Figuras Cariocineticas: *Ibid.*, XLIV. — **Gardiner, E. G.**, **'98.** The Growth of the Ovum, *etc.*, in Polychœrus: *J. M.*, XV., 1. — **Gardiner, W.**, **'83.** Continuity of Protoplasm in Vegetable Cells: *Phil. Trans.*, CLXXIV. — **Garnault**, **'88**, **'89.** Sur les phénomènes de la fécondation chez Helix aspera et Arion empiricorum: *Zoöl. Anz.*, XI., XII. — **Geddes and Thompson.** The Evolution of Sex: *London*, 1899. — — **Gegenbaur, C.**, **'54.** Beiträge zur näheren Kenntniss der Schwimmpolypen: *Z. w. Z.*, V. — **Van Gehuchten, A.**, **'90.** Recherches histologiques sur l'appareil digestif de la larve de la Ptychoptera contaminata: *La Cellule*, VI. — **Giard, A.**, **'77.**

Sur la signification morphologique des globules polaires: *Revue scientifique*, XX. — **Id.**, '**90**. Sur les globules polaires et les homologues de ces éléments chez les infusoires ciliés: *Bulletin scientifique de la France et de la Belgique*. XXII. — **Godlewsky, E.**, '**97, 1**. Über mehrfache bipolar Mitose bei der Spermatogenese von Helix: *Anz. Akad. Wiss. Krakau*. — **Id.**, '**97, 2**. Weitere Untersuchungen über die Umwandlung der Spermatiden, *etc.*: *Anz. Akad. Wiss. Krakau.*, Nov., '97. — **Goroschanktin, J.**, '**83**. Zur Kenntniss der Corpuscula bei den Gymnospermen: *Bot. Zeit.*, LXI. — **Graf, A.**, '**97**. The Individuality of the Cell: *N. Y. State Hosp. Bull.*, April. — **Grégoire, V.**, '**99**. Les cinèses polliniques dans les Liliacées: *Bot. Centb.*, XX., 1; *La Cellule*, XVI., 2. — **Griffin, B. B.**, '**96**. The History of the Achromatic Structures in the Maturation and Fertilization of *Thalassema*: *Trans. N. Y. Acad. Sci.* — **Id.**, '**99**. Studies on the Maturation, Fertilization, and Cleavage of Thalassema and Zirphæa: *J. M.*, XV. — **Gierke, H.**, '**85**. Färberei zu mikroskopischen Zwecken: *Zeit. Wiss. Mik.*, II. — **Grobben, C.**, '**78**. Beiträge zur Kenntniss der männlichen Geschlechtsorgane der Dekapoden: *Arb. Zoöl. Inst. Wien*, I. — **Gruber, A.**, '**84**. Über Kern und Kerntheilung bei den Protozoen: *Z. w. Z.*, XL. — **Id.**, '**85**. Über künstliche Teilung bei Infusorien: *B. C.*, IV., 23; V., 5. — **Id.**, '**86**. Beiträge zur Kenntniss der Physiologie und Biologie der Protozoen: *Ber. Naturf. Ges. Freiburg*, I. — **Id.**, '**93**. Mikroscopische Vivisektion: *Ber. d. Naturf. Ges. zu Freiburg*, VII., 1. — **Id.**, '**97**. Weitere Beobachtungen an vielkernigen Infusorien: *Ber. Naturf. Ges. Freiburg*, III. — **Guignard, L.**, '**89**. Développement et constitution des Anthérozoides: *Rev. gen. Bot.*, I. — **Id.**, '**91, 1**. Nouvelles études sur la fécondation: *Ann. d. Sciences Nat. Bot.*, XIV. — **Id.**, '**91, 2**. Sur l'existence des "sphères attractives" dans les cellules végétales: *C.R.*, 9 Mars. — **Id.**, '**98, 1**. Les centres cinétiques chez les végétaux: *Ann. Sci. Nat. Bot.*, (VIII.) V.; also, *Bot. Gaz.*, XXV. — **Id.**, '**98, 2**. Le developpement du pollen et la réduction chromatique dans le *Nais major*: *Arch. Anat. Mik.*, II., 4. — **Id.**, '**99**. Sur les anthérozoides et la double copulation sexuelle chez les végétaux angiospermes: *C. R.*, CXXVIII., 14.

HABERLANDT, G., '**87**. Über die Beziehungen zwischen Funktion und Lage des Zellkerns: *Fischer*, 1887. — **Häckel, E.**, '**66**. Generelle Morphologie. — **Id.**, '**91**. Anthropogenie, 4th ed., *Leipzig*, 1891. — **Häcker, V.**, '**92, 1**. Die Furchung des Eies von Æquorea Forskalea: *A. m. A.*, XL. — **Id.**, '**92, 2**. Die Eibildung bei Cyclops und Canthocamptus: *Zool. Jahrb.*, V. — **Id.**, '**92, 3**. Die heterotypische Kerntheilung im Cyclus der generativen Zellen: *Ber. naturf. Ges. Freiburg*, VI. — **Id.**, '**93**. Das Keimbläschen, seine Elemente und Lageveränderungen: *A. m. A.*, XLI. — **Id.**, '**94**. Über den heutigen Stand der Centrosomenfrage: *Verhandl. d. deutschen Zool. Ges.*, 1894, p. 11. — **Id.**, '**95, 1**. Die Vorstadien der Eireifung: *A. m. A.*, XLV., 2. — **Id.**, '**95, 2**. Zur frage nach dem Vorkommen der Schein-Reduktion bei den Pflanzen: *Ibid.*, XLVI. Also *Ann. Bot.*, IX. — **Id.**, '**95, 3**. Über die Selbständigkeit der väterlichen und mütterlichen Kernsbestandtheile während der Embryonalentwicklung von Cyclops: *A. m. A.*, XLVI., 4. — **Id.**, '**97, 1**. Die Keimbahn von Cyclops: *A. m. A.*, XLIX. — **Id.**, '**97, 2**. Über weitere Übereinstimmungen zwischen den Fortpflanzungsvorgängen der Thiere und Pflanzen: *B. C.*, XVII. — **Id.**, '**98**. Über vorbereitende Theilungsvorgänge bei Thieren und Pflanzen: *Verh. d. Zool. Ges.*, VIII. — **Id.**, '**99**. Praxis und Theorie der Zellen und Befruchtungslehre: *Jena, Fischer.* — **Hallez, P.**, '**86**. Sur la loi de l'orientation de l'embryon chez les insectes: *C. R.*, 103, 1886. — **Halliburton, W. D.**, '**91**. A Text-book of Chemical Physiology and Pathology: *London.* — **Id.**, '**93**. The Chemical Physiology of the Cell: (*Gouldstonian Lectures*) *Brit. Med. Journ.* — **Hammar, J. A.**, '**96**. Über einen primären Zusammenhang zwischen den Furchungszellen des Seeigeleies: *A. m. A.*, XLVII., 1. — **Id.**, '**97**. Über eine allgemein vorkommende primäre Protoplasmaverbindung zwischen den Blastomeren: *A. m. A.*, XLIX. — **Hammarsten, O., '94.** Zur Kenntniss der Nucleoproteiden: *Zeit. Phys. Chem.*, XIX. — **Id., '95.** Lehrbuch der physiologischen Chemie, 3e Ausgabe: *Wiesbaden*, 1895. — **Hansemann, D., '91.** Karyokinese und Cellularpathologie: *Berl. Klin. Wochenschrift*, No. 42. — **Id., '93.** Spezificität, Altruismus und die Anaplasie der Zellen: *Berlin*, 1893. — **Hanstein, J., '80.** Das Protoplasma als Träger der pflanzlichen und thierischen Lebensverrichtungen. *Heidelberg.* — **Harper, R. A., '96.** Über das Verhalten der Kerne bei der Fruchtentwickelung einiger Ascomyceten: *Jahrb. wiss. Bot.*, XXIX. — **Id., '97.** Kernteilung und freie Zellbildung im Ascus: *Ibid.*, XXX. — **Hardy, W. B., '99.** On the Structure of Cell-protoplasm: *Jour. Phys.*, XXIV., 2. — **Harvey, Wm., 1651.** Exercitationes de Generatione Animalium: *London.* Trans. in *Sydenham Soc.*, X., 1847. — **Hartog, M. M., '91.** Some Problems of Reproduction, etc.: *Q. J.*, XXXIII. — **Id., '96.** The Cytology of Saprolegnia: *Ann. Bot.*, IX. — **Id., '98.** Nuclear Reduction and the Function of Chromatin: *Nat. Sci.*, XII. — **Hatschek, B., '87.** Über die Bedeutung der geschlechtlichen Fortpflanzung: *Prager Med. Wochenschrift*, XLVI. — **Id., '88.** Lehrbuch der Zoologie. — **Heath, H., '99.** The Development of Ischnochiton: *Jena, Fischer.* — **Heidenhain, M., '93.** Über Kern und Protoplasma: *Festchr. z. 50-Jähr. Doctorjub. von v. Kölliker: Leipzig.* — **Id., '94.** Neue Untersuchungen über die Centralkörper und ihre Beziehungen zum Kern und Zellenprotoplasma: *A. m. A.*, XLIII. — **Id., '95.** Cytomechanische Studien: *A. Entwm.*, I., 4. — **Id., '96, 1.** Ein neues Modell zum Spannungsgesetz der centrirten Systeme: *Verh. anat. Ges.* — **Id., '96, 2.** Über die Mikrocentren mehrkerniger Riesenzellen, etc.: *Morph. Arb.*, VII., 1. — **Id., '99.** Über eine eigenthümliche Art Knospung an Epithelzellen, etc.: *A. m. A.*, LIV., 1. — **Heidenhain and Cohn,' 97.** Über die Mikrocentren in den Geweben des Vogelembryos, etc.: *Morph. Arb.*, VII. — **Heitzmann, J., '73.** Untersuchungen über das Protoplasma: *Sitz. d. k. Acad. Wiss. Wien.*, LXVII. — **Id., '83.** Mikroscopische Morphologie des Thierkörpers im gesunden und kranken Zustande: *Wien*, 1883. — **Henking, H.** Untersuchungen über die ersten Entwicklungsvorgänge in den Eiern der Insekten, I., II., III.: *Z. w. Z.*, XLIX., LI., LIV., 1890-92. — **Henle, J., '41.** Allgemeine Anatomie: *Leipzig.* — **Henneguy, L. F., '91.** Nouvelles recherches sur la division cellulaire indirecte: *Journ. Anat. et Physiol.*, XXVII. — **Id., 93.** Le Corps vitellin de Balbiani dans l'œuf des Vértébres: *Ibid.*, XXIX. — **Id., '96.** Leçons sur la cellule: *Paris.* — **Id., '98.** Sur les rapports des cils vibratils avec les centrosomes: *Arch. Anat. Mik.*, I. — **Hensen, V., '81.** Physiologie der Zeugung: *Hermann's Physiologie*, VI. — **Herbst, C.** Experimentelle Untersuchungen über den Einfluss der veränderten chemischen Zusammensetzung des umgebenden Mediums auf die Entwicklung der Thiere, I.; *Z. w. Z.*, LV., 1892; II., *Mitt. Zool. St. Neapel*, XI., 1893; III.-VI., *Arch. Entwm.*, II., 4, 1896. — **Id., '94, '95.** Über die Bedeutung der Reizphysiologie für die Kausale Auffassung von Vorgängen in der tierischen Ontogenese: *Biol. Centralb.*, XIV., XV., 1894, 1895. — **Herla, V., '93.** Étude des variations de la mitose chez l'ascaride mégalocéphale: *A. B.*, XIII. — **Herlitzka, A., '95.** Contributo allo studio della capacità evolutiva dei due primi blastomeri nell' uove di Tritone: *A. Entwm.*, II., 3. — **Hermann, F., '89.** Beiträge zur Histologie des Hodens: *A. m. A.*, XXXIV. — **Id., '91.** Beitrag zur Lehre von der Entstehung der karyokinetischen Spindel: *Ibid.*, XXXVII. — **Id., '92.** Urogenitalsystem, Struktur und Histiogenese der Spermatozoen: *Merkel und Bonnet's Ergebnisse*, II. — **Id., '97.** Beiträge zur Kenntniss der Spermatogenese: *A. m. A.*, L. — **Hertwig, O., '75.** Beiträge zur Kenntniss der Bildung, Befruchtung und Teilung des tierischen Eies, I.: *M. J.*, I. — **Id., '77.** Beiträge, etc., II.; *Ibid.*, III. — **Id., '78.** Beiträge, etc., III.; *Ibid.*, IV. — **Id., '84.** Das Problem der Befruchtung und der Isotropie des Eies, eine Theorie der Vererbung: *J. Z.*, XVIII. — **Id., '90, 1.** Vergleich der Ei- und Samenbildung bei Nematoden. Eine

Grundlage für celluläre Streitfragen: *A. m. A.*, XXXVI. — **Id.**, **'90, 2.** Experimentelle Studien am tierischen Ei vor, während und nach der Befruchtung: *J. Z.*, 1890. — **Id.**, **'92, 1.** — Urmund und Spina Bifida: *A. m. A.*, XXXIX. — **Id.**, **92, 2.** Aeltere und neuere Entwicklungs-theorieen: *Berlin.* — **Id.**, **'93, 1.** Über den Werth der ersten Furchungszellen für die Organbildung des Embryo: *A. m. A.*, XLII, — **Id.**, **93, 2.** Die Zelle und die Gewebe: *Fischer, Jena*, 1893, 1898. — **Id.**, **'94.** Zeit und Streitfragen der Biologie: *Berlin.* — **Hertwig, O.** and **R.**, **'86.** Experimentelle Untersuchungen über die Bedingungen der Bastardbefruchtung: *J. Z.*, XIX. — **Id.**, **'87.** Über den Befruchtungs- und Teilungsvorgang des tierischen Eies unter dem Einfluss äusserer Agentien: *Ibid.*, XX. — **Hertwig, R.**, **'77.** Über den Bau und die Entwicklung der Spirochona gemmipara: *Ibid.*, XI. — **Id.**, **'84.** Die Kerntheilung bei Actinosphærium Eichhorni: *Ibid.*, XVII. — **Id.**, **'88.** Über Kernstruktur und ihre Bedeutung für Zellteilung und Befruchtung: *Ibid.*, IV., 1888. — **Id.**, **'89.** Über die Konjugation der Infusorien: *Abh. der bayr. Akad. d. Wiss.*, II., Cl., XVII. — **Id.**, **'92.** Über Befruchtung und Conjugation: *Verh. deutsch. Zool. Ges.*, *Berlin.* — **Id.**, **'95.** Über Centrosoma und Centralspindel: *Sitz.-Ber. Ges. Morph. und Phys.*, *München*, 1805, Heft I. — **Id.**, **'96.** Über die Entwicklung des unbefruchteten Seeigeleies, etc.: *Festchr. f. Gegenbaur.* — **Id.**, **'97, 1.** Über die Bedeutung der Nucleolen: *Sitzb. Ges. Morph. Phys. München*, 1898, I. — **Id.**, **'97, 2.** — Über Karyokinese bei Actinosphærium: *Sitzb. Ges. Morph. Phys. München*, XIII., 1. — **Id.**, **'98.** Kerntheilung, Richtungskörperbildung und Befruchtung von Actinosphærium: *Abh. K. bayer. Akad. Wiss.*, XIX, 2. — **Heuser, E.**, **'84.** Beobachtung über Zelltheilung: *Bot. Cent.* — **Hill, M. D.**, **'95.** Notes on the Fecundation of the Egg of *Sphærechinus granularis* and on the Maturation and Fertilization of the Egg of *Phallusia mammillata*: *Q. J.*, XXXVIII. — **Hirase, S.**, **'97.** Untersuchungen über das erhalten des Pollens von Gingko biloba: *Bot. Centb.*, LXIX., 2, 3. — **Id.**, **'98.** Études sur la fécondation et l'embryogénie der Gingko: *Jour. Coll. Sci.*, *Tokio*, XII. — **His, W.**, **'74.** Unsere Körperform und das physiologische Problem ihrer Entstehung: *Leipzig.* — **Hofer, B.**, **'89.** Experimentelle Untersuchungen über den Einfluss des Kerns auf das Protoplasma: *J. Z.*, XXIV. — **Hoffman, R. W.**, **'98.** Über Zellplatten und Zellplattenrudimente: *Z. w. Z.*, LXIII. — **Hofmeister**, **'67.** Die Lehre von der Pflanzenzelle: *Leipzig*, 1867. — **Holl, M.**, **'90.** Über die Reifung der Eizelle des Huhns: *Sitzb. Acad. Wiss. Wien*, XCIX., 3. — **Hooke, Robt.**, **1665.** Mikrographia, or some physiological Descriptions of minute Bodies by magnifying Glasses: *London.* — **Hoyer, H.**, **'90.** Über ein für das Studium der "direkten" Zelltheilung vorzüglich geeignetes Objekt: *A. A.*, V. — **Hubbard, J. W.**, **'94.** The Yolk-Nucleus in Cymatogaster: *Proc. Am. Phil. Soc.*, XXXIII. — **Huie, L.**, **'97.** Changes in the Cell-organs of *Drosera* produced by Feeding with Egg-albumen: *Q. J.*, XXXIX. — **Humphrey, J. E.**, **'94.** Nucleolen und Centrosomen: *Ber. deutschen bot. Ges.*, XII., 5. — **Id.**, **'95.** On some Constituents of the Cell: *Ann. Bot.*, IX. — **Huxley, T. H.**, **'53.** Review of the Cell-theory: *Brit. and Foreign Med.-Chir. Review*, XII. — **Id.**, **'78.** Evolution in Biology, *Enc. Brit.*, 9th ed., 1878; *Science and Culture*, N. Y., 1882.

IKENO, S., **'97.** Vorläufige Mitth. über die Spermatozoiden bei Cycas: *Bot. Centb.*, LXIX., 1. — **Id.**, **'98, 1.** Zur Kenntniss des sogenannten centrosomähnlichen Körpers im Pollenschläuche der Cycaden: *Flora*, LXXXV., 1. — **Id.**, **'98, 2.** Untersuchungen über die Entwickelung der Geschlechtsorgane, *etc.*, bei *Cycas*: *Jahrb. wiss. Bot.*, XXXII., 4. — **Ishikawa, M.**, **'91.** Vorläufige Mitteilungen über die Konjugationserscheinungen bei den Noctiluceen: *Z. A.*, No. 353, 1891. — **Id.**, **'94.** Studies on Reproductive Elements: II., *Noctiluca miliaris* Sur., Its Division and Spore-formation: *Journ. College of Sc. Imp. Univ. Japan*, VI. — **Id.**, **'97.** Die

Entwickelung der Pollenkörner von Allium: *Journ. Coll. Sci. Tokyo*, X., 2. — **Id.**, **'99.** Further Observations on the Nuclear Division of Noctiluca: *Ibid.*, XII., 4.

JENNINGS, H. S., '96. The Early Development of Asplanchna: *Bull. Mus. Comp. Zoöl.*, XXX. — **Jensen, O. S., '83.** Recherches sur la spermatogénèse: *A. B.*, IV. — **Johnson, H. P., '92.** Amitosis in the embryonal envelopes of the Scorpion: *Bull. Mus. Comp. Zoöl.*, XXII., 3. — **Jordan, E. O., '93.** The Habits and Development of the Newt: *J. M.*, VIII., 2. — **Jordan and Eycleshymer, '94.** On the Cleavage of Amphibian Ova: *J. M.*, IX., 3, 1894. — **Juel, H. O., '97.** Die Kerntheilungen in den Pollenmutterzellen, *etc.*: *Jahrb. wiss. Bot.*, XXX. — **Julin, J., '93, 1.** Structure et développement des glandes sexuelles, ovogénèse, spermatogénèse et fécondation chez Styleopsis grossularia: *Bull. Sc. de France et de Belgique*, XXIV. — **Id., '93, 2.** Le corps vitellin de Balbiani et les éléments des Métazoaires qui correspondent au Macronucléus des Infusoires ciliés: *Ibid.*, XXIV.

KARSTEN, G., '96. Untersuchungen über Diatomeen: *Flora*, LXXXII. — **Keuten, J., '95.** Die Kerntheilung von *Euglena viridis* Ehr: *Z. w. Z.*, LX. — **Kienitz-Gerloff, F., '91.** Review and Bibliography of Researches on Protoplasmic Connection between adjacent Cells: in *Bot. Zeitung*, XLIX. — **Kingsbury, B. F., '99.** The Reducing Divisions in the Spermatogenesis of Desmognathus: *Zoöl. Bull.*, II., 5. — **Klebahn, '90.** Die Keimung von Closterium und Cosmarium: *Jahrb. wiss. Bot.*, XXII. — **Id., '92.** Die Befruchtung von Œdigonium: *Jahrb. f. wiss. Bot.*, XXIV. — **Id., '96.** Beiträge zur Kenntniss der Auxosporenbildung, I., Rhopalodia: *Jahrb. wiss. Bot.*, XXIX. — **Klebs, G., '83.** Über die Organisation einiger Flagellaten-Gruppen, etc.: *Bot. Inst. Tübingen*, I., 1. — **Id., '84.** Über die neueren Forschungen betreffs der Protoplasmaverbindungen benachbarter Zellen: *Bot. Zeit.*, 188.4 — **Id., '87.** Über den Einfluss des Kerns in der Zelle: *B. C.*, VII. — **Klein, E., '78–'79.** Observations on the Structure of Cells and Nuclei: *Q. J.*, XVIII., XIX. — **Klinckowström, A. v., '97.** Beiträge zur Kenntniss der Eireife und Befruchtung bei Prostheceræus: *A. m. A.*, XLVIII. — **von Kölliker, A., '41.** Beiträge zur Kenntniss der Geschlechtsverhältnisse und der Samenflüssigkeit wirbelloser Tiere: *Berlin*. — **Id., '44.** Entwicklungsgeschichte der Cephalopoden: *Zürich*. — **Id., '85.** Die Bedeutung der Zellkerne für die Vorgänge der Vererbung: *Z. w. Z.*, XLII. — **Id., '86.** Das Karyoplasma und die Vererbung, eine Kritik der Weismann'schen Theorie von der Kontinuität des Keimplasmas: *Ibid.*, XLIII. — **Id., '89.** Handbuch der Gewebelehre, 6th ed.: *Leipzig*. — **Id., '97.** Die Energiden von Sachs, *etc.*: *Verh. Phys. Med. Ges.*, *Würzburg*, XXXI., 5. — **Korff, '99.** Zur Histogenese der Spermien von Helix: *A. m. A.*, LIV. **Korschelt, E., '89.** Beiträge zur Morphologie und Physiologie des Zell-kernes: *Zoöl. Jahrb. Anat. u. Ontog.*, IV. — **Id., '93.** Über Ophryotrocha puerilis: *Z. w. Z.*, LIV. — **Id., '95.** Über Kerntheilung, Eireifung und Befruchtung bei *Ophryotrocha puerilis*: *Ibid.*, LX. — **Id., '96.** Kernstructuren und Zellmembranen in den Spinndrüsen der Raupen: *A. m. A.*, XLVII. — **Id., '97.** Über den Bau der Kerne in den Spinndrüsen der Raupen: *Ibid.*, XLIX. — **Kossel, A., '91.** Über die chemische Zusammensetzung der Zelle: *Arch. Anat. u. Phys.* — **Id., '93.** Über die Nucleinsäure: *Ibid.*, 1893. — **Id., '96.** Über die basischen Stoffe des Zellkernes: *Zeit. Phys. Chem.*, XXII. — **von Kostanecki, K., '91.** Über Centralspindelkörperchen bei karyokinetischer Zellteilung: *Anat. Hefte*, 1892, dat. 91. — **Id., '96.** Über die Gestalt der Centrosomen im befruchteten Seeigelei: *Ibid.*, VII., 2. — **Id., '97, 1.** Über die Bedeutung der Polstrahlung, *etc.*: *A. m. A.*, LXIX. — **Id., '98.** Die Befruchtung des Eies von *Myzostoma*: *Ibid.*, LI. — **Kostanecki and Siedlecki, '96.** Über das Verhalten der Centrosomen zum Protoplasma: *Ibid.*, XLIX. — **Kostanecki and Wierzejski, '96.** Über das Verhalten der sogenannten achromatischen Substanzen im befruchteten Ei: *Ibid.*, XLII., 2. — **Kühne, W., '64.** Untersuchungen über das Protoplasma und die Contractilität. — **Kupffer, C.**, '75. Über Differenzierung des Protoplasma an den Zellen thierischer Gewebe: *Schr. natur. Ver. Schles.-Holst.*, I., 3. — **Id.**, '90. Die Entwicklung von Petromyzon Planeri: *A. m. A.*, XXXV. — **Id.**, '96. Über Energiden und paraplastische Bildungen: *Rektoratrede*, *München*, 1896.

LAMEERE, A., '90. Recherches sur la reduction karyogamique: *Bruxelles.* — **Lauterborn, R.**, '93. Über Bau und Kerntheilung der Diatomeen: *Verh. d. Naturh. Med. Ver. in Heidelberg*, 1893. — **Id.**, '95. · Protozoenstudien, Kern- und Zellteilung von Ceratium hirundinella O. F. M.: *Z. w. Z.*, XLIX. — **Id.**, '96. — **La Valette St. George**, '65. Über die Genese der Samenkörper: *A. m. A.*, I. — **Id.**, '67. Über die Genese der Samenkörper, II. (Terminology): *Ibid.*, III. — **Id.**, '76. Die Spermatogenese bei den Amphibien: *Ibid.*, XII. — **Id.**, '78. Die Spermatogenese bei den Säugethieren und dem Menschen: *Ibid.*, XV. — **Id.**, '85–'87. Spermatologische Beiträge, I.–V.: *Ibid.*, XXV., XXVII., XXVIII., and XXX. — **Lankester, E. Ray**, '77. Notes on Embryology and Classification: *London.* — **Lavdovsky, M.**, '94. Von der Entstehung der chromatischen und achromatischen Substanzen in den tierischen und pflanzlichen Zellen: *Merkel und Bonnet's Anat. Hefte*, IV., 13. — **Lawson, A. A.**, '98. Some Observations on the Development of the Karyokinetic Spindle, *etc.*: *Proc. Cal. Acad. Sci.*, I., 5. — **Lazarus, A.**, '98. Die Anæmie: *Wien.* — **Lee, A. Bolles**, '96. Sur le Nebenkern, *etc.*, chez Helix: *La Cellule*, XI. — **Id.**, '97. Les cinèses spermatogénétiques chez Helix: *Ibid.*, XIII. — **von Lenhossék, M.**, '95. Centrosom und Sphäre in den Spinalganglien des Frosches: *A. m. A.*, XLVI. — **Id.**, '98, **1**. Über Flimmerzellen: *Verh. An. Ges.*, XII. — **Id.**, '98, **2**. Untersuchungen über Spermatogenesis: *A. m. A.*, LI. — **Id.**, '99. Das Mikrocentrum der glatten Muskelzellen: *A. A.*, XVI., 13, 14. — **Leydig, Fr.**, '54. Lehrbuch der Histologie des Menschen und der Thiere: *Frankfurt.* — **Id.**, '85. Zelle und Gewebe, *Bonn.* — **Id.**, '89. Beiträge zur Kenntniss des thierischen Eies im unbefruchteten Zustande: *Spengel's Jahrb. Anat. Ont.*, III. — **Lilienfeld, L.**, '92, '93. Über die Verwandtschaft der Zellelemente zu gewissen Farbstoffen: *Verh. Phys. Ges., Berlin*, 1892–93. — **Id.**, '93. Über die Wahlverwandtschaft der Zellelemente zu Farbstoffen: *A. A. P.*, 1893. — **Lillie, F. R.**, '95. The Embryology of the Unionidæ: *J. M.*, X. — **Id.**, '96. On the Smallest Parts of Stentor capable of Regeneration: *J. M.*, XII., 1. — **Id.**, '97. On the Origin of the Centres of the First Cleavage-spindle in Unio: *Science*, V. — **Id.**, '98. Centrosome and Sphere in the Egg of Unio: *Zoöl. Bull.*, I., 6. — **Id.**, '99. Adaptation in Cleavage: *Wood's Holl Biol. Lect.* — **List, Th.**, '96. Beiträge zur Chemie der Zelle und Gewebe, I.: *Mitth. Zoöl. St. Neap.*, XII., 3. — **Loeb, J.**, '91–'92. Untersuchungen zur physiologischen Morphologie. I. Heteromorphosis: *Würzburg*, 1891. II. Organbildung und Wachsthum: *Ibid.*, 1892. — **Id.**, '92. Experiments on Cleavage: *J. M.*, VII. — **Id.**, '93. Some Facts and Principles of Physiological Morphology: *Wood's Holl Biol. Lectures*, 1893. — **Id.**, '94. Über die Grenzen der Theilbarkeit der Eisubstanz: *A. ges. P.*, LIX., 6, 7. — **Id.**, '95. Über Kerntheilung ohne Zelltheilung: *Arch. Entwm.*, II. — **Id.**, '99, **1**. Warum ist die Regeneration kernloser Protoplasmastücken unmöglich, *etc.*: *Ibid.*, VIII., 4. — **Id.**, '99, **2**. On the Nature of the Process of Fertilization and the Artificial Production of Normal Larvæ, *etc.*: *Am. Journ. Phys.*, III., 3. — **Löwit, M.**, '91. Über amitotische Kerntheilung: *B. C.*, XI. — **Lukjanow**, '91. Grundzüge einer allgemeinen Pathologie der Zelle: *Leipzig.* — **Lustig and Galeotti**, '93. Cytologische Studien über pathologische menschliche Gewebe: *Beitr. Path. Anat.*, XIV.

MACALLUM, A. B., '91. Contribution to the Morphology and Physiology of the Cell: *Trans. Canad. Inst.*, I., 2. — **McClung, C. E.**, '99. A Peculiar Nuclear Element in the Male Reproductive Cells of Insects: *Zoöl. Bull.*, II., 4. — **MacFar-**

land, F. M., '97. Celluläre Studien an Molluskeneiern: *Zoöl. Jahrb. Anat.*, X. — **McGregor, J. H.**, '99. The Spermatogenesis of Amphiuma: *J. M.*, XV., Suppl. — **McMurrich, J. P.**, '86. A Contribution to the Embryology of the Prosobranch Gasteropods: *Studies Biol. Lab. Johns Hopkins Univ.*, III. — **Id.**, '95. Embryology of the Isopod Crustacea: *J. M.*, XI., 1. — **Id.**, '96. The Yolk-Lobe and the Centrosome of Fulgur: *A. A.*, XII., 23. — **Id.**, '97. The Epithelium of the Midgut of the Terrestrial Isopods: *J. M.*, XIV., 1. — **Maggi, L.**, '78. I plastiduli nei ciliati ed i plastiduli liberamente viventi: *Atti. Soc. Ital. Sc. Nat. Milano*, XXI. (also later papers). — **Malfatti, H.**, '91. Beiträge zur Kenntniss der Nucleine: *Zeit. Phys. Chem.*, XVI. — **Mark, E. L.**, '81. Maturation, Fecundation, and Segmentation of Limax campestris: *Bull. Mus. Comp. Zoöl. Harvard College*, VI. — **Mathews, A. P.**, '97, 1. Internal Secretions considered in Relation to Variation and Development: *Science*, V., 122. — **Id.**, '97, 2. Zur Chemie der Spermatozoen: *Zeit. Phys. Chem.*, XXIII., 4, 5. — **Id.**, '98. A Contribution to the Chemistry of Cytological Staining: *Am. Journ. Phys.*, I., 4. — **Id.**, '99, 1. The Origin of Fibrinogen: *Ibid.*, III. — **Id.**, '99, 2. The Metabolism of the Pancreas Cell: *J. M.*, XV., Suppl. — **Maupas, M.**, '88. Recherches expérimentales sur la multiplication des Infusoires ciliés: *Arch. Zoöl. Exp.*, 2me série, VI. — **Id.**, '89. Le rejeunissement karyogamique chez les Ciliés: *Ibid.*, 2me série, VII. — **Id.**, '91. Sur le déterminisme de la sexualité chez l'Hydatina senta: *C. R., Paris.* — **Mayer, P.**, '91. Über das Färben mit Carmin, Cochenille und Hämatein-Thonerde: *Mitth. Zoöl. St. Neapol.*, X., 3. — **Id.**, '97. Beruht die Färbung der Zellkerne auf einem chemischen Vorgang oder nicht?: *A. A.*, XIII., 12. — **Mead, A. D.**, '95. Some Observations on Maturation and Fecundation in Chætopterus pergamentaceus Cuv.: *J. M.*, X., 1. — **Id.**, '97, 1. The Origin of the Egg-centrosomes: *Ibid.*, XII. — **Id.**, '97. 2. The early Development of marine Annelids: *Ibid.*, V. — **Id.**, '98, 1. The Origin and Behaviour of the Centrosomes in the Annelid Egg: *Ibid.*, XIV., 2. — **Id.**, '98, 2. The Rate of Cell-division and the Function of the Centrosome: *Wood's Holl Biol. Lectures.* — **Merkel, F.**, '71. Die Stützzellen des menschlichen Hodens: *Müller's Arch.* — **Mertens, H.**, '93. Recherches sur la signification du corps vitellin de Balbiani dans l'ovule des Mammifères et des Oiseaux: *A. B.*, XIII. — **Metschnikoff, E.**, '66. Embryologische Studien an Insecten: *Z. w. Z.*, XVI. — **Meves, F.**, '91. Über amitotische Kernteilung in den Spermatogonien des Salamanders, und das Verhalten der Attraktionssphären bei derselben: *A. A.*, 1891, No. 22. — **Id.**, '94. Über eine Metamorphose der Attraktionssphäre in den Spermatogonien von Salamandra maculosa: *A. m. A.*, XLIV. — **Id.**, '95. Über die Zellen des Sesambeines der Achillessehne des Frosches (*Rana temporaria*) und über ihre Centralkörper: *Ibid.*, XLV. — **Id.**, '96. Über die Entwicklung der männlichen Geschlechtszellen von Salamandra: *Ibid.*, XLVIII. — **Id.**, '97, 1. Zur Struktur der Kerne in den Spinndrüsen der Raupen: *Ibid.*, XLVIII. — **Id.**, '97, 2. Über Struktur und Histiogenese der Samenfäden von Salamandra: *Ibid.*, L. — **Id.**, '97, 3. Über den Vorgang der Zelleinschnürung: *Arch. Entwm.*, V., 2. — **Id.**, '97, 4. Zelltheilung: *Merkel u. Bonnet, Erg.*, VI. — **Id.**, '97, 5. Über Centralkörper in männlichen Geschlechtszellen von Schmetterlingen: *A. A.*, XIV., 1. — **Id.**, '98. Über das Verhalten der Centralkörper bei der Histogenese der Samenfäden vom Mensch und Ratte: *Verh. An. Ges.*, XIV. — **Id.**, '99. Über Struktur und Histogenesis der Samenfäden des Meerschweinschens: *A. m. A.*, LIV. — **Meyer, A.**, '96. Die Plasmaverbindungen, *etc.*: *Bot. Zeit.*, 11, 12. — **Meyer, O.**, '95. Cellular-Untersuchungen an Nematodeneiern: *J. Z.*, XXIX. (XXII.). — **Michaelis, L.**, '97. Die Befruchtung des Tritoneies: *A. m. A.*, XLVIII. — **Miescher, F.**, '96. Physiologisch-chemische Untersuchungen über die Lachsmilch: *Arch. Exp. Path. u. Pharm.*, XXXVII. — **Mikosch**, '94. Über Struktur im pflanzlichen Protoplasma: *Verhandl. d. Ges. deutscher Naturf. und Arzte*, 1894; *Äbteil f. Pflanzen-*

physiologie u. Pflanzenanatomie. — **Minot, C. S., '77.** Recent Investigations of Embryologists: *Proc. Bost. Soc. Nat. Hist.*, XIX. — **Id., '79.** Growth as a Function of Cells: *Ibid.*, XX. — **Id., '82.** Theorie der Genoblasten: *B. C.*, II., 12. See also *Am. Nat.*, February, 1880, and *Proc. Bost. Soc. Nat. Hist.*, XIX., 1877. — **Id., '91.** Senescence and Rejuvenation: *Journ. Phys.*, XII., 2. — **Id., '92.** Human Embryology: *New York.* — **von Mohl Hugo, '46.** Über die Saftbewegung im Innern der Zellen: *Bot. Zeitung.* — **Moll, J. W., '93.** Observations on Karyokinesis in Spirogyra: *Verh. Kon. Akad.*, *Amsterdam*, No. 9. — **Montgomery, Th. H., '98, 1.** The Spermatogenesis of Pentatoma, *etc.*: *Zoöl. Jahrb.* — **Id., '98, 2.** Comparative Cytological Studies, with Especial Reference to the Morphology of the Nucleolus: *J. M.*, XV., 2. — **Moore, J. E. S., '93.** Mammalian Spermatogenesis: *A. A.*, VIII. — **Id., '95.** On the Structural Changes in the Reproductive Cells during the Spermatogenesis of Elasmobranchs: *Q. J*, XXXVIII. — **Morgan, T. H., '93.** Experimental Studies on Echinoderm Eggs: *A. A.*, IX., 5, 6. — **Id., '95, 1.** Studies of the "Partial" Larvæ of Sphærechinus: *A. Entwm.*, II., 1. — **Id., '95, 2.** Experimental Studies on Teleost-eggs: *A. A.*, X., 19. — **Id., '95, 3.** Half-embryos and Whole-embryos from one of the first two Blastomeres of the Frog's Egg: *Ibid.*, X., 19. — **Id., '95, 4.** The Fertilization of non-nucleated Fragments of Echinoderm-eggs: *Arch. Entwm.*, II., 2. — **Id., '95, 5.** The Formation of the Fish-embryo: *J. M.*, X., 2. — **Id., '96, 1.** On the Production of artificial archoplasmic Centres: *Rept. of the Am. Morph. Soc.*, *Science*, III., January 10, 1896. — **Id., '96, 2.** The Number of Cells in Larvæ from Isolated Blastomeres of Amphioxus: *Arch. Entwm.*, III., 2. — **Id., '96, 3.** The Production of Artificial Astrosphæres: *Arch. Entwm.*, III. — **Id., '98, 1.** Experimental Studies of the Regeneration of Planaria maculata: *Ibid.*, VII., 2, 3. — **Id., '98, 2.** Regeneration and Liability to Injury: *Zoöl. Bull.*, I., 6. — **Id., '99, 1.** The Action of Salt-solutions on the Unfertilized and Fertilized Eggs of *Arbacia* and other Animals: *Arch. Entwm.*, VIII., 3. — **Id., '99, 2.** A Confirmation of Spallanzani's Discovery, *etc.*: *A. A.*, XV. 21. — **Mottier, D. M., '97, 1.** Über das Verhalten der Kerne bei der Entwicklung des Embryosacs, *etc.*: *Jahrb. wiss. Bot.*, XXXI. — **Id., '97, 2.** Beiträge zur Kenntniss der Kerntheilung in den Pollenmutterzellen, *etc.*: *Ibid.*, XXX. — **Id., '98.** Das Centrosoma bei Dictyota: *Ber. D. Bot. Ges.*, XVI., 5. — **Müller, E., '96.** Über die Regeneration der Augenlinse nach Exstirpation derselben bei Triton: *A. m. A.*, XLVII., 1. — **Munson, J. P., '98.** The Ovarian Egg of Limulus, *etc.*: *J. M.*, XV., 2. — **Murray, J. A., '98.** Contributions to a Knowledge of the Nebenkern in the Spermatogenesis of Pulmonata: *Zoöl. Jahrb.*, XI., 14.

NADSON, G., '95. Über den Bau des Cyanophyceen-Protoplastes: *Script. Botan. Horti. Petropol.*, IV. — **Nägeli, C., '84.** Mechanisch-physiologische Theorie der Abstammungslehre: *München u. Leipzig*, 1884. — **Nägeli und Schwendener, '67.** Das Mikroskop. (See later editions.) *Leipzig.* — **Nawaschin, '99.** Neue Beobachtungen über Befruchtung bei *Fritillaria* und *Lilium*: *Bot. Centb.*, LXXVII., 2. — **Nemec, B., '97.** Über die Struktur der Diplopodeneier, *A. A.*, XIII., 10, 11. — **Id., '99.** Über die karyokinetische Kerntheilung in den Würzelspitzen von *Allium*: *J. w. B.*, XXVIII, 2. — **Newport, G.** On the Impregnation of the Ovum in the Amphibia: *Phil. Trans.*, 1851, 1853, 1854. — **Norman, W. W., '96.** Segmentation of the Nucleus without Segmentation of the Protoplasm: *Arch. Entwm.*, III. — **Nussbaum, M., '80.** Zur Differenzierung des Geschlechts im Tierreich: *A. m. A.*, XVIII. — **Id., '84, 1.** Über Spontane und Künstliche Theilung von Infusorien: *Verh. d. naturh. Ver. preus.*, *Rheinland*, 1884. — **Id., '84, 2.** Über die Veränderungen der Geschlechtsproducte bis zur Eifurchung: *A. m. A.*, XXIII. — **Id., '85.** Über die Teilbarkeit der lebendigen Materie, I.: *A. m. A.*, XXVI. —

Id., **'94.** Die mit der Entwickelung fortschreitende Differenzierung der Zellen: *Sitz.-Ber. d. niederrhein. Gesellschaft f. Natur- u. Heilkunde, Bonn*, 5 Nov., 1894; also *B. C.*, XVI., 2, 1896. — **Id.**, **'97.** Die Entstehung des Geschlechts bei Hydatina: *A. m. A.*, XLIX.

OBST, P., **'99.** Untersuchungen über das Verhalten der Nucleolen, etc.: *Z. w. Z.* LXVI., 2. — **Ogata, '83.** Die Veränderungen der Pancreaszellen bei der Secretion: *A. A. P.* — **Oppel, A.**, **'92.** Die Befruchtung des Reptilieneies: *A. m. A.* XXXIX. — **Osterhout, W. J. V.**, **'97.** Über Entstehung der karyokinetischen Spindel bei Equisetum: *Jahrb. wiss. Bot.*, XXX. — **Oltmanns, F.**, **'95.** Über die Entwickelung der Sexualorgane bei *Vaucheria*: *Flora*. — **Overton, C. E.**, **'88.** Über den Conjugationsvorgang bei Spirogyra: *Ber. deutsch. Bot. Ges.*, VI. — **Id.**, **'89.** Beitrag zur Kenntniss der Gattung Volvox: *Bot. Centralb.*, XXXIX. — **Id.**, **'93.** Über die Reduktion der Chromosomen in den Kernen der Pflanzen: *Vierteljahrschr. naturf. Ges. Zürich*, XXXVIII. Also *Ann. Bot.*, VII., 25.

PALADINO, G., **'90.** I ponti intercellulari tra l' uovo ovarico e le cellule follicolari, etc.: *A. A.*, V. — **Paulmier, F. C.**, **'98.** Chromatin Reduction in the Hemiptera: *A. A.*, XIV. — **Id.**, **'99.** The Spermatogenesis of Anasa tristis: *J. M.*, XV., Suppl. — **Peter, K.**, **'99.** Das Centrum für die Flimmer- und Geisselbewegung: *A. A.*, XV., 14, 15. — **Pfeffer, W.**, **'99.** Über die Erzeugung und die physiologische Bedeutung der Amitose: *Ber. königl., sächs., Ges. Wiss. Leipzig.*, July 3. — **Pfitzner, W.**, **'82.** Über den feineren Bau der bei der Zelltheilung auffretenden fadenförmigen Differenzierungen des Zellkerns: *M. J.*, VII. — **Id.**, **'83.** Beiträge zur Lehre vom Baue des Zellkerns und seinen Theilungserscheinungen: *A. m. A.*, XXII. — **Pflüger, E.**, **'83.** Über den Einfluss der Schwerkraft auf die Theilung der Zellen: I., *Arch. ges. Phys.*, XXXI.; II., *Ibid.*, XXXII.; abstract in *Biol. Centb.*, III., 1884. — **Id.**, **'84.** Über die Einwirkung der Schwerkraft und anderer Bedingungen auf die Richtung der Zelltheilung: *Arch. ges. Phys.*, XXXIV. — **Id.**, **'89.** Die allgemeinen Lebenserscheinungen: *Bonn*. — **Platner, G.**, **'86, 1.** Zur Bildung der Geschlechtsprodukte bei den Pulmonaten: *A. m. A.*, XXVI. — **Id.**, **'86, 2.** — Über die Befruchtung von *Arion empiricorum*: *A. m. A.*, XXVII. — **Id.**, **'89, 1.** Über die Bedeutung der Richtungskörperchen: *B. C.*, VIII. — **Id.**, **'89, 2.** Beiträge zur Kenntniss der Zelle und ihrer Teilungserscheinungen, I.–VI.: *A. m. A.*, XXXIII. — **Poirault and Raciborski, '96.** Über konjugate Kerne und die konjugate Kerntheilung: *B. C.*, XVI., 1. — **Prenant, A.**, **'94.** Sur le corpuscule central: *Bull. Soc. Sci.*, *Nancy*, 1894. — **Id.**, **'98, '99.** Sur le protoplasma supérieure (archoplasme, kinoplasme, ergastoplasme): *Jour. Anat. Phys.*, XXXIV., XXXV. — **Preusse, F.**, **'95.** Über die amitotische Kerntheilung in den Ovarien der Hemipteren: *Z. w. Z.*, LIX., 2. — **Prévost and Dumas, '24.** Nouvelle théorie de la génération: *Ann. Sci. Nat.*, I., II. — **Pringsheim, N.**, **'55.** Über die Befruchtung der Algen: *Monatsb. Berl. Akad.*, 1855–56.

RABL, C., **'85.** Über Zellteilung: *M. J.*, X. — **Id.**, **'89, 1.** Über Zelltheilung: *A. A.*, IV. — **Id.**, **'89, 2.** Über die Prinzipien der Histologie: *Verh. Anat. Ges.*, III. — **vom Rath, O.**, **'91.** Über die Bedeutung der amitotischen Kernteilung im Hoden: *Zoöl. Anz.*, XIV. — **Id.**, **'92.** Zur Kenntniss der Spermatogenese von *Gryllotalpa vulgaris*: *A. m. A.*, XL. — **Id.**, **'93.** Beiträge zur Spermatogenese von Salamandra: *Z. w. Z.*, LVII. — **Id.**, **'94.** Über die Konstanz der Chromosomenzahl bei Tieren: *B. C.*, XIV., 13. — **Id.**, **'95, 1.** Neue Beiträge zur Frage der Chromatinreduction in der Samen- und Eireife: *A. m. A.*, XLVI. — **Id.**, **'95, 2.** Über den feineren Bau der Drüsenzellen des Kopfes von Anilocra, etc.: *Z. w. Z.*, LX., 1. — **Rauber, A.**, **'83.** Neue Grundlegungen zur Kenntniss der Zelle: *M. J.*,

VIII. — **Rawitz, B.**, **'95.** Centrosoma und Attraktionsphäre in der ruhenden Zelle des Salamanderhodens: *A. m. A.*, XLIV., 4. — **Id.**, **'97.** Bemerkungen über Mikrotomschneiden, etc.: *A. A.*, XIII. — **Reinke, Fr.**, **'94.** Zellstudien, I., *A. m. A.*, XLIII.: III., *Ibid.*, XLIV., 1894. — **Id.**, **'95.** Untersuchungen über Befruchtung und Furchung des Eies der Echinodermen: *Sitz.-Ber. Akad. d. Wiss. Berlin*, 1895, June 20. — **Reinke and Rodewald, '81.** Studien über das Protoplasma: *Untersuch. aus. d. bot. Inst. Göttingen*, II. — **Remak, R.**, **'41.** Über Theilung rother Blutzellen beim Embryo: *Med. Ver. Zeit.*, 1841. — **Id.**, **'50–'55.**, Untersuchungen über die Entwicklung der Wirbelthiere: *Berlin*, 1850–55. — **Id.**, **'58.** Über die Theilung der Blutzellen beim Embryo: *Müller's Arch.*, 1858. — **Retzius, G.**, **'89.** Die Intercellularbrücken des Eierstockeies und der Follikelzellen: *Verh. Anat. Ges.*, 1889. — **Rhumbler, L.**, **'93.** Über Entstehung und Bedeutung der in den Kernen vieler Protozoen und im Keimbläschen von Metazoen vorkommenden Binnenkörper (Nucleolen): *Z. w. Z.*, LVI. — **Id.**, **'96.** Versuch einer mechanischen Erklärung der indirekten Zell- und Kerntheilung: *Arch. Entwm.*, III. — **Id.**, **'97.** Stemmen die Strahlen der Astrosphäre oder ziehen sie? *Arch. Entwm.*, IV. — **Rompel, '94.** Kentrochona Nebaliæ n. sp., ein neues Infusor aus der Familie der Spirochoninen. Zugleich ein Beitrag zur Lehre von der Kernteilung und dem Centrosoma: *Z. w. Z.*, LVIII., 4. — **Rosen, '92.** Über tinctionelle Unterscheidung verschiedener Kernbestandtheile und der Sexual-kerne: *Cohn's Beitr. z. Biol. d. Pflanzen*, V. — **Id.**, **'94.** Neueres über die Chromatophilie der Zellkerne: *Schles. Ges. väterl. Kult.*, 1894. — **Roux, W.**, **'83, 1.** Über die Bedeutung der Kernteilungsfiguren: *Leipzig*. — **Id.**, **'83, 2.** Über die Zeit der Bestimmung der Hauptrichtungen des Froschembryo: *Leipzig*. — **Id.**, **'85.** Über die Bestimmung der Hauptrichtungen des Froschembryos im Ei, und über die erste Theilung des Froscheies: *Breslauer ärtzl. Zeitg.*, 1885. — **Id.**, **'87.** Bestimmung der medianebene des Froschembryo durch die Kopulationsrichtung des Eikernes und des Spermakernes: *A. m. A.*, XXIX. — **Id.**, **'88.** Über das künstliche Hervorbringen halber Embryonen durch Zerstörung einer der beiden ersten Furchungskugeln, etc.: *Virchow's Archiv*, 114. — **Id.**, **'90.** Die Entwickelungsmechanik der Organismen. *Wien*, 1890. — **Id.**, **'92, 1.** Entwickelungsmechanik: *Merkel and Bonnet, Erg.*, II. — **Id.**, **'92, 2.** Über das entwickelungsmechanische Vermögen jeder der beiden ersten Furchungszellen des Eies: *Verh. Anat. Ges.*, VI. — **Id.**, **'93, 1.** Über Mosaikarbeit und neuere Entwickelungshypothesen: *An. Hefte*, Feb., 1893. — **Id.**, **'93, 2.** Über die Spezifikation der Furchungzellen, etc.: *B. C.*, XIII., 19–22 — **Id.**, **'94, 1.** Über den "Cytotropismus" der Furchungszellen des Grasfrosches: *Arch. Entwm.*, I., 1, 2. — **Id.**, **'94, 2.** Aufgabe der Entwickelungsmechanik, etc.: *Arch. Entwm.*, I., 1. Trans. in *Biol. Lectures, Wood's Holl*, 1894. — **Rückert, J.**, **'91.** Zur Befruchtung des Selachiereies: *A. A.*, VI. — **Id.**, **'92, 1.** Zur Entwicklungsgeschichte des Ovarialeies bei Selachiern: *A. A.*, VII. — **Id.**, **'92, 2.** Über die Verdoppelung der Chromosomen im Keimbläschen des Selachiereies: *Ibid.*, VIII. — **Id.**, **'93, 2.** Die Chromatinreduktion der Chromosomenzahl im Entwicklungsgang der Organismen: *Merkel and Bonnet, Erg.*, III. — **Id.**, **'94.** Zur Eireifung bei Copepoden: *An. Hefte*. — **Id.**, **'95, 1.** Zur Kenntniss des Befruchtungsvorganges: *Sitsb. Bayer. Akad. Wiss.*, XXVI., 1. — **Id.**, **'95, 2.** Zur Befruchtung von *Cyclops strenuus: A. A.*, X., 22. — **Id.**, **'95, 3.** Über das Selbständigbleiben der väterlichen und mütterlichen Kernsubstanz während der ersten Entwicklung des befruchteten Cyclops-Eies: *A. m. A.*, XLV., 3. — **Rüge, G.**, **'89.** Vorgänge am Eifollikel der Wirbelthiere: *M. J.*, XV. — **Ryder, J. A.**, **'83.** The Microscopic Sexual Characteristics of the Oyster, etc., *Bull. U. S. Fish. Comm.*, March 14, 1883. Also, *Ann. Mag. Nat. Hist.*, XII., 1883.

SABASCHNIKOFF, M., '97. Beiträge zur Kenntniss der Chromatinreduktion in der Ovogenesis von Ascaris: *Bull. Soc. Nat., Moscow,* 1. — **Sabatier, A., '90.** De la Spermatogénèse chez les Locustides: *Comptes Rend.,* CXI., '90. — **Sachs, J., '82.** Vorlesungen über Pflanzen-physiologie: *Leipzig.* — **Id.** Über die Anordnung der Zellen in jüngsten Pflanzentheile: *Arb. Bot. Inst. Würzburg,* II. — **Id., '92.** Physiologische Notizen, II., Beiträge zur Zellentheorie: *Flora,* 1892, Heft I. — **Id., '93.** Stoff und Form der Pflanzen-organe: *Gesammelte Abhandlungen,* II., 1893. — **Id., '95.** Physiologische Notizen, IX., weitere Betrachtungen über Energiden und Zellen: *Flora,* LXXXI., 2. — **Sala, L., '95.** Experimentelle Untersuchungen über die Reifung und Befruchtung der Eier bei *Ascaris megalocephala: A. m. A.,* XL. — **Sargant, Ethel, '95.** Some details of the first nuclear Division in the Pollen-mother-cells of *Lilium martagon: Journ. Roy. Mic. Soc.,* 1895, part 3. — **Id., '96.** The Formation of the Sexual Nuclei in Lilium, I., Oogenesis: *Ann. Bot.,* X. — **Id., '97.** Same title, II., Spermatogenesis: *Ibid.,* XI. — **Schäfer, E. A., '91.** General Anatomy or Histology: in *Quain's Anatomy,* I., 2, 10th ed., London. — **Schaffner, J. H., '97, 1.** The Life-history of Sagittaria: *Bot. Gaz.,* XXIII., 4. — **Id., '97, 2.** The Division of the Macrospore Nucleus (in Lilium): *Ibid.,* XXIII., 6. — **Id., '98.** Karyokinesis in Root-tips of Allium: *Ibid.,* XXVI., 4. — **Schaudinn, F., '95.** Über die Theilung von *Amœba binucleata* Gruber: *Sitz.-Ber. Ges. Naturforsch. Freunde, Berlin,* Jahrg. 1895, No. 6. — **Id., '96, 1.** Über den Zeugungskreis von *Paramœba Eilhardi: Sitz.-Ber. Akad. Wiss., Berlin,* 1896, Jan. 16. — **Id., '96, 2.** Über die Copulation von Actinophrys Sol: *Ibid.* — **Id., '96, 3.** Über das Centralkorn der Heliozoen: *Verh. D. Zoöl. Ges.* — **Schewiakoff, W., '88.** Über die karyokinetische Kerntheilung der *Euglypha alveolata: M. J.,* XIII. — **Id., '93.** Über einen neuen Bakterienähnlichen Organismus: *Hab. Schrift, Heidelberg, Winter.* — **Schiefferdecker and Kossel, '91.** Die Gewebe des Menschlichen Körpers: *Braunschweig.* — **Schimper, '85.** Untersuchungen über die Chlorophyllkörper, *etc.: Zeitsch. wiss. Bot.,* XVI. — **Schleicher, W., '78.** Die Knorpelzelltheilung. Ein Beitrag zur Lehre der Theilung von Gewebezellen: *Centr. med. Wiss. Berlin,* 1878. Also *A. m. A.,* XVI., 1879. — **Schleiden, M. J., '38.** Beiträge zur Phytogenesis: *Müller's Archiv,* 1838. [Trans. in *Sydenham Soc.,* XII.: *London,* 1847.] — **Schloter, G., '94.** Zur Morphologie der Zelle: *A. m. A.,* XLIV., 2. — **Schmitz, '84.** Die Chromatophoren der Algen. — **Schneider, A., '73.** Untersuchungen über Plathelminthen: *Jahrb. d. oberhess. Ges. f. Natur-Heilkunde,* XIV., *Giessen.* — **Schneider, C., '91.** Untersuchungen über die Zelle: *Arb. Zoöl. Inst. Wien,* IX., 2. — **Schottländer, J., '88.** Über Kern und Zelltheilungsvorgänge in dem Endothel der entzündeten Hornhaut: *A. m. A.,* XXXI. — **Schottländer, P., '93.** Beiträge zur Kenntniss des Zellkerns, *etc.: Cohn's Beiträge,* VI. — **Schultze, Max, '61.** Über Muskelkörperchen und das was man eine Zelle zu nennen hat: *Arch. Anat. Phys.,* 1861. — **Schultze, O., '87.** Untersuchungen über die Reifung und Befruchtung des Amphibien-eies: *Z. w. Z.,* XLV. — **Id., '90.** Über Zelltheilung: *Sitzb. phys. med. Ges. Würzburg.* — **Id., '94.** Die künstliche Erzeugung von Doppelbildungen bei Froschlarven, *etc.: Arch. Entwm.,* I., 2. — **Schwann, Th., '39.** Mikroscopische Untersuchungen über die Übereinstimmung in der Structur und dem Wachsthum der Thiere und Pflanzen: *Berlin.* [Trans. in *Sydenham Soc.,* XII.: *London,* 1847.] — **Schwarz, Fr., '87.** Die Morphologische und chemische Zusammensetzung des Protoplasmas: *Breslau.* — **Schweigger-Seidel, O., '65.** Über die Samenkörperchen und ihre Entwickelung: *A. m. A.,* I. — **Sedgwick, A., '85-'88.** The Development of the Cape Species of Peripatus, I.-VI.: *Q. J.,* XXV.-XXVIII. — **Id., '94.** On the Inadequacy of the Cellular Theory of Development, *etc.: Ibid.,* XXXVII., 1. — **Seeliger, O., '94.** Giebt es geschlechtlicherzeugte Organismen ohne mütterliche Eigenschaften?: *A. Ent.,* I., 2. — **Selenka, E., '83.** Die Keimblätter der Echinodermen: *Studien*

über Entwick., II., *Wiesbaden*, 1883. — **Sertoli, E., '65.** Dell' esistenza di particolari cellule ramificate dei canaliculi seminiferi del testicolo umano: *Il Morgagni.* — **Shaw, W. R., '98, 1.** Über die Blepharoplasten bei Onoclea und Marsilia: *Ber. D. Bot. Ges.*, XVI., 7. — **Id., '98, 2.** The Fertilization of Onoclea: *Ann. Bot.*, XII., 47. — **Siedlecki, M., '95.** Über die Struktur und Kerntheilungsvorgänge bei den Leucocyten der Urodelen: *Anz. Akad. Wiss.*, *Krakau*, 1895. — **Id., '99.** Étude cytologique et cycle évolutif de Adelea: *Ann. Inst. Pasteur.*, XIII. — **Sobotta, J., '95.** Die Befruchtung und Furchung des Eies der Maus: *A. m. A.*, XLV. — **Id., '97.** Die Reifung und Befruchtung des Eies von Amphioxus: *Ibid.*, L. — **Solger, B., '91.** Die radiären Strukturen der Zellkörper im Zustand der Ruhe und bei der Kerntheilung: *Berl. Klin. Wochenschr.*, XX., 1891. — **Spallanzani, 1786.** Expériences pour servir à l'histoire de la génération des animaux et des plantes: *Geneva.* — **Spitzer, '97.** Die Bedeutung gewisser Nucleoproteide für die oxydative Leistung der Zelle: *Arch. ges. Phys.*, LXVII. — **Stevens, W. C., '98.** Über Chromosomentheilung bei der Sporenbildung der Farne: *Ber. D. Bot. Ges.*, XVI., 8. — **Stevens, F. L., '99.** The compound Oösphere of Albugo: *Bot. Gaz.*, XXVIII., 3, 4. — **Strasburger, E., '75.** Zellbildung und Zelltheilung: 1st ed., *Jena*, 1875. — **Id., '77.** Über Befruchtung und Zelltheilung: *J. Z.*, XI. — **Id., '80.** Zellbildung und Zellteilung: 3d ed. — **Id., '82.** Über den Theilungsvorgang der Zellkerne und das Verhältniss der Kerntheilung zur Zelltheilung: *A. m. A.*, XXI. — **Id., '84, 1.** Die Controversen der indirecten Zelltheilung: *Ibid.*, XXIII. — **Id., '84, 2.** Neue Untersuchungen über den Befruchtungsvorgang bei den Phanerogamen, als Grundlage für eine Theorie der Zeugung: *Jena*, 1884. — **Id., '88.** Über Kern- und Zellteilung im Pflanzenreich, nebst einem Anhang über Befruchtung: *Jena.* — **Id., '89.** Über das Wachsthum vegetabilischer Zellhäute: *Hist. Bei.*, II., *Jena.* — **Id., '91.** Das Protoplasma und die Reizbarkeit: *Rektoratsrede*, *Bonn*, Oct. 18, 1891. *Jena*, *Fischer.* — **Id., '92.** Histologische Beiträge, Heft IV.: Das Verhalten des Pollens und die Befruchtungsvorgänge bei den Gymnospermen, Schwärmsporen, pflanzliche Spermatozoiden und das Wesen der Befruchtung: *Fischer*, *Jena*, 1892. — **Id., '93, 1.** Über die Wirkungssphäre der Kerne und die Zellengrösse: *Hist. Beitr.*, V. — **Id., '93, 2.** Zu dem jetzigen Stande der Kern- und Zelltheilungsfragen: *A. A.*, VIII., p. 177. — **Id., '94.** Über periodische Reduktion der Chromosomenzahl im Entwicklungsgang der Organismen: *B. C.*, XIV. — **Id., '95.** Karyokinetische Probleme: *Jahrb. f. wiss. Botanik*, XXVIII., 1. — **Id., '97, 1.** Kerntheilung und Befruchtung bei Fucus: *Jahrb. wiss. Bot.*, XXX. — **Id., '97, 2.** Über Befruchtung: *Ibid.* — **Id., '97, 3.** Über Cytoplasmastrukturen, Kern- und Zelltheilung: *Ibid.* — **Id., '98.** Die Pflanzlichen Zellhäute: *Ibid.*, XXXI. — **Strasburger and Mottier, '97.** Über den zweiten Theilungsschritt in Pollenmutterzellen: *Ber. D. Bot. Ges.*, XV., 6. — **Van der Stricht, O., '92.** Contribution à l'étude de la sphère attractive: *A. B.*, XII., 4. — **Id., '95, 1.** La maturation et la fécondation de l'œuf d'Amphioxus lanceolatus: *Bull. Acad. Roy. Belgique*, XXX., 2. — **Id., '95, 2.** De l'origine de la figure achromatique de l'ovule en mitose chez le Thysanozoon Brocchi: *Verhandl. d. anat. Versamml. in Strassburg*, 1895, p. 223. — **Id., '95, 3.** Contributions à l'étude de la forme, de la structure et de la division du noyau: *Bull. Acad. Roy. Sc. Belgique*, XXIX. — **Id., '98, 1.** La formation des globules polaires, *etc.*, chez Thysanozoon: *Arch. Biol.*, XV. — **Id., '98, 2.** Contribution à l'étude du noyau vitellin de Balbiani: *Verh. An. Ges.*, XII. — **Stricker, S., '71.** Handbuch der Lehre von den Geweben: *Leipzig.* — **Stuhlmann, Fr., '86.** Die Reifung des Arthropodeneies nach Beobachtungen an Insekten, Spinnen, Myriopoden und Peripatus: *Ber. Naturf. Ges. Freiburg*, I. — **Suzuki, B., '98.** Notiz über die Entstehung des Mittelstückes von Selachiern: *A. A.*, XV., 8. — **Swaen and Masquelin, '83.** Étude sur la Spermatogénèse: *A. B.*, IV. — **Swingle, W. T., '97.** Zur Kenntniss der Kern- und Zellteilungen bei den Sphacelariaceæ: *J. w. B.*, XXX.

THOMA, R., '96. Text-book of General Pathology and Pathological Anatomy: Trans. by A. Bruce, *London.* — **Thomson, Allen.** Article "Generation" in Todd's Cyclopædia. — **Id.** Article "Ovum" in Todd's Cyclopædia. — **Townsend, C. O., '97.** Der Einfluss des Zellkerns auf die Bildung der Zellhaut: *Jahrb. wiss. Bot.*, XXX. — **Treat, Mary, '73.** Controlling Sex in Butterflies: *Am. Nat.*, VII. — **Trow, A. H., '95.** The Karyology of Saprolegnia: *Ann. Bot.*, IX. — **Tyson, James, '78.** The Cell-doctrine: 2d ed., *Philadelphia.*

UNNA, P., '95. Über die neueren Protoplasmatheorien, und das Spongioplasma: *Deutsche Med. Zeit.*, 1895, 98–100. — **Ussow, M., '81.** Untersuchungen über die Entwickelung der Cephalopoden: *Arch. Biol.*, II.

VEJDOVSKÝ, F., '88. Entwickelungsgeschichtliche Untersuchungen, Heft I.: Reifung, Befruchtung und Furchung des Rhynchelmis-Eies: *Prag*, 1888. **Vejdovský and Mrázek, '98.** Centrosom und Periplast: *Sitzber. böhm. Ges. Wiss.* — **Verworn, M., '88.** Biologische Protisten-studien: *Z. w. Z.*, XLVI. — **Id., '89.** Psychophysiologische Protisten-studien: *Jena.* — **Id., '91.** Die physiologische Bedeutung des Zellkerns: *Pflüger's Arch. f. d. ges. Physiol.*, II. — **Id., '95.** Allgemeine Physiologie: *Jena.* — **Virchow, R., '55.** Cellular-Pathologie: *Arch. Path. Anat. Phys.*, VIII., 1. — **Id., '58.** Die Cellularpathologie in ihrer Begründung auf physiologische und pathologische Gewebelehre: *Berlin*, 1858. — **De Vries, H., '89.** Intracelluläre Pangenesis: *Jena.*

WAGER, H., '96. On the Structure and Reproduction of Cystopus. *Ann. Bot.*, X. — **Waldeyer, W., '70.** Eierstock und Ei: *Leipzig.* — **Id., '87.** Bau und Entwickelung der Samenfäden: *Verh. An. Ges. Leipzig*, 1887. — **Id., '88.** Über Karyokinese und ihre Beziehungen zu den Befruchtungsvorgängen: *A. m. A.*, XXXII. [Trans. in *Q. J.*] — **Id., '95.** Die neueren Ansichten über den Bau und das Wesen der Zelle: *Deutsch. Med. Wochenschr.*, No. 43, ff., Oct. ff., 1895. — **Warneck, N. A., '50.** Über die Bildung und Entwickelung des Embryos bei Gasteropoden: *Bull. Soc. Imp. Nat. Moscou*, XXIII., 1. — **Watasé, S., '91.** Studies on Cephalopods; I., Cleavage of the Ovum: *J. M.*, IV., 3. — **Id., '92.** On the Phenomena of Sex-differentiation: *Ibid.*, VI., 2, 1892. — **Id., '93, 1.** On the Nature of Cell-organization: *Wood's Holl Biol. Lectures*, 1893. — **Id., '93, 2.** Homology of the Centrosome: *J. M.*, VIII., 2. — **Id., '94.** Origin of the Centrosome: *Biological Lectures, Wood's Holl*, 1894. **Webber, H. J., '97, 1.** Peculiar Structures occurring in the Pollen-tube of Zamia: *Bot. Gazette*, XXIII., 6. — **Id., '97, 2.** The Development of the Antherozoids of Zamia: *Ibid.*, XXIV., 1. — **Id., '97, 3.** Notes on the Fecundation of Zamia and the Pollen-tube Apparatus of Gingko: *Ibid.*, XXIV., 4. — **Weismann, A., '83.** Über Vererbung: *Jena.* — **Id., '85.** Die Kontinuität des Keimplasmas als Grundlage einer Theorie der Vererbung: *Jena.* — **Id., '86, 1.** Richtungskörper bei parthenogenetischen Eiern: *Zool. Anz.*, No. 233. — **Id., '86, 2.** Die Bedeutung der sexuellen Fortpflanzung für die Selektionstheorie: *Jena.* — **Id., '87.** Über die Zahl der Richtungskörper und über ihre Bedeutung für die Vererbung: *Jena.* — **Id., '91, 1.** Essays upon Heredity. First Series: *Oxford.* — **Id., '91, 2.** Amphimixis, oder die Vermischung der Individuen: *Jena, Fischer.* — **Id., '92.** Essays upon Heredity, Second Series: *Oxford*, 1892. — **Id., '93.** The Germ-plasm: *New York.* — **Id., '94.** Äussere Einflüsse als Entwicklungsreize: *Jena.* — **Id., '99.** Regeneration: *Nat. Sci.*, XIV., 6. [See also *A. A.*, 1899.] **Wheeler, W. M., '89.** The Embryology of *Blatta Germanica* and *Doryphora decemlineata*: *J. M.*, III. — **Id., '93.** A Contribution to Insect-embryology: *Ibid.*, VIII., 1. — **Id., '95.** The Behaviour of the Centrosomes in the Fertilized Egg of *Myzostoma glabrum*: *Ibid.*, X. — **Id., '96.** The Sexual Phases of Myzostoma:

Mitth. Zool. St. Neapel, XII., 2. — **Id.**, **'97.** The Maturation, Fecundation, and early Cleavage in Myzostoma: *Arch. Biol.*, XV. — **Whitman, C. O.**, **'78.** The Embryology of Clepsine: *Q. J.*, XVIII. — **Id.**, **'87.** The Kinetic Phenomena of the Egg during Maturation and Fecundation: *J. M.*, I., 2. — **Id.**, **'88.** The Seat of Formative and Regenerative Energy: *Ibid.*, II. — **Id.**, **'93.** The Inadequacy of the Cell-theory of Development: *Wood's Holl Biol. Lectures*, 1893. — **Id.**, **'94.** Evolution and Epigenesis: *Ibid.*, 1894. — **Wiesner, J.**, **'92.** Die Elementarstruktur und das Wachstum der lebenden Substanz: *Wien.* — **Wilcox, E. V.**, **'95.** Spermatogenesis of Caloptenus and Cicada: *Bull. of the Museum of Comp. Zoöl., Harvard College*, Vol. XXVII., No. 1. — **Id.**, **'96.** Further Studies on the Spermatogenesis of Caloptenus: *Bull. Mus. Comp. Zoöl.*, XXIX. — **Will, L.**, **'86.** Die Entstehung des Eies von Colymbetes: *Z. w. Z.*, XLIII. — **Wilson, Edm. B.**, **'92.** The Cell-lineage of *Nereis*: *J. M.*, VI., 3. — **Id.**, **'93.** Amphioxus and the Mosaic Theory of Development: *Ibid.*, VIII., 3. — **Id.**, **'94.** The Mosaic Theory of Development: *Wood's Holl Biol. Lect.*, 1894. — **Id.**, **'95, 1.** Atlas of Fertilization and Karyokinesis: *New York, Macmillan.* — **Id.**, **'95, 2.** Archoplasm, Centrosome, and Chromatin in the Sea-urchin Egg: *J. M.*, XI. — **Id.**, **'96.** On Cleavage and Mosaic-work. [Appendix to Crampton and Wilson, '96.]: *A. Entwm.*, III., 1. — **Id.**, **'97.** Centrosome and Middle-piece in the Fertilization of the Egg. *Science*, Vol. V., No. 114. — **Id.**, **'98.** Considerations on Cell-lineage and ancestral Reminiscence: *Ann. N. Y. Acad. Sci.*, XI. See also *Wood's Holl Biol. Lectures*, '99. — **Id.**, **'99.** On protoplasmic Structure in the Eggs of Echinoderms and some other Animals: *J. M.*, XV. Suppl. — **Wilson and Mathews**, **'95.** Maturation, Fertilization, and Polarity in the Echinoderm Egg: *J. M.*, X., 1. — **Wolff, Caspar Friedrich, 1759.** Theoria Generationis. — **Wolff, Gustav**, **'94.** Bemerkungen zum Darwinismus mit einem experimentellen Beitrag zur Physiologie der Entwicklung: *B. C.*, XIV., 17. — **Id.**, **'95.** Die Regeneration der Urodelenlinse: *Arch. Entwm.*, I., 3. — **Wolters, M.**, **'91.** Die Conjugation und Sporenbildung bei Gregarinen: *A. m. A.*, XXXVII. — **Woltereck, R.**, **'98.** Zur Bildung und Entwicklung des Ostrakoden-Eies: *Z. w. Z.*, LXIV.

YUNG, E., **'81.** De l'influence de la nature des aliments sur la sexualité: *C. R.*, XCIII; also *Arch. Exp. Zool.*, 2d, I., 1883.

ZACHARIAS, O., **'85.** Über die amöboiden Bewegungen der Spermatozoen von Polyphemus pediculus: *Z. w. Z.*, XLI. — **Zacharias, E.**, **'93, 1.** Über die chemische Beschaffenheit von Cytoplasma und Zellkern: *Ber. deutsch. Bot. Ges.*, II., 5. — **Id.**, **'93, 2.** Über Chromatophilie: *Ibid.*, 1893. — **Id.**, **'95.** Über das Verhalten des Zellkerns in wachsenden Zellen: *Flora*, 81, 1895. — **Id.**, **'94.** Über Beziehungen des Zellenwachstums zur Beschaffenheit des Zellkerns: *Berichte der deutschen botan. Gesellschaft*, XII., 5. — **Id.**, **'98.** Über Nachweis und Vorkommen von Nuclein: *Ber. d. Bot. Ges.*, XVI., 7. — **Ziegler, E.**, **'88.** Die neuesten Arbeiten über Vererbung und Abstammungslehre und ihre Bedeutung für die Pathologie: *Beitr. zur path. Anat.*, IV. — **Id.**, **'89.** Über die Ursachen der pathologischen Gewebsneubildungen: *Int. Beitr. zur. wiss. Med. Festschrift. R. Virchow*, II. — **Id.**, **'92.** Lehrbuch der allgemeinen pathologischen Anatomie und Pathogenese, 7th ed., *Jena.* — **Ziegler, H. E.**, **'87.** Die Entstehung des Blutes bei Knochenfischenembryonen: *A. m. A.* — **Id.**, **'91.** Die biologische Bedeutung der amitotischen Kerntheilung im Tierreich: *B. C.*, XI. — **Id.**, **'94.** Über das Verhalten der Kerne im Dotter der meroblastischen Wirbelthiere: *Ber. Naturf. Ges. Freiburg*, 1894. — **Id.**, **'95.** Untersuchungen über die Zelltheilung: *Verhandl. d. deutsch. Zool. Ges.*, 1895. — **Id.**, **'96.** Einige Betrachtungen zur Entwicklungsgeschichte der Echinodermen: *Verh. d. Zool. Ges.* — **Id.**, **'98.** Experimentelle Studien über die Zelltheillung, I., II.: *Arch. Entwm.*, VI., 2. — **Ziegler and vom Rath.** Die amitotische Kerntheilung bei den Arthropoden: *B. C.*, XI. — **Zimmermann, A., '93, 1.** Beiträge zur Morphologie und Physiologie der Pflanzenzelle: *Tübingen.* — **Id., '94.** Sammelreferate aus dem Gesammtgebiete der Zellenlehre: *Bot. Centb. Beihefte*, 1894. **Zimmermann, K. W., '93, 2.** Studien über Pigmentzellen, etc.: *A. m. A.*, XLI. — **Id., '98.** Beiträge zur Kenntniss einiger Drüsen und Epithelzellen: *A. m. A.*, LII. — **Zoja, R., '95, 1.** Sullo sviluppo dei blastomeri isolati dalle uova di alcune meduse: *A. Entwm.*, I., 4; II., 1; II., IV. — **Id., '95. 2.** Sulla independenza della cromatina paterna e materna nel nucleo delle cellule embrionali: *A. A.*, XI., 10. **Id., '97.** Stato attuale degli Studii sulla Fecondazione: *Boll. Sci. di Pavia*, XVIII., XIX. — **Zur Strassen, O., '98.** Über die Riesenbildung bei Ascaris-Eiern: *Arch. Entwm.*, VII., 4.

INDEX OF AUTHORS

Albrecht, nuclei, 32.
Altmann, granule-theory, 25, 27, 290; nuclein, 332.
Amici, pollen-tube, 218.
Andrews, spinning activities, 61.
Apathy, nerve-cells, 48.
Aristotle, epigenesis, 8.
Arnold, fibrillar theory of protoplasm, 23; leucocytes, 117; nucleus and cytoplasm, 303.
Atkinson, reduction, 269.
Auerbach, 6; double spermatozoa, 142; staining-reactions, 176; fertilization, 181.

Von Baer, cleavage, 10; cell-division, 64; egg-axis, 378; development, 396.
Balbiani, scattered nuclei, 40; spireme-nuclei, 36; mitosis in Infusoria, 88; chromatin-granules, 112; yolk-nucleus, 155–156; regeneration in Infusoria, 343.
Balfour, polar bodies, 243; rate of division, 366; unequal division, 371.
Ballowitz, structure of spermatozoa, 139, 140; double spermatozoa, 142.
Van Bambeke, deutoplasm and yolk-nucleus, 156–160; elimination of chromatin, 155.
Barry, fertilization, 181.
De Bary, protoplasm, 4, 5, 20; conjugation, 181; cell-division and growth, 393.
Beale, cell-organization, 291.
Béchamp and Estor, microsome-theory, 290, 291.
Belajeff, spermatozoids, 172–175; reduction in plants, 267.
Benda, spermatogenesis, 163; Sertoli-cells, 284.
Van Beneden, cell-theory, 1, 6, 7; protoplasm, 23; nuclear membrane, 38; centrosome and attraction-sphere, 51, 74, 77, 310, 323; cell-polarity, 55; cell-division, 64, 74; origin of mitotic figure, 74–77; theory of mitosis, 100; division of chromosomes, 112; fertilization of *Ascaris*, 7, 182; continuity of centrosomes, 75; germ-nuclei, 205; centrosome in fertilization, 208; theory of sex, 243; parthenogenesis, 281; nucleus and cytoplasm, 303; nuclear microsomes, 302; promorphology of cleavage, 381; germinal localization, 399.
Van Beneden and Julin, first cleavage-plane, 380.
Bergmann, cleavage, 10; cell, 17.
Bernard, Claude, nucleus and cytoplasm, 341; organic synthesis, 431.
Berthold, protoplasm, 42; cell-division, 376.
Bickford, regeneration in cœlenterates, 392, 429.
Biondi, Sertoli-cells, 284.
Biondi-Ehrlich, staining-fluid, 157.
Bischoff, cell, 17.
Bizzozero, cell-bridges, 60.
Blanc, fertilization of trout, 210.
Blochmann, insect-egg, 132; budding of nucleus, 155; polar bodies, 281; bilaterality of ovum, 383.
Böhm, fertilization in fishes, 192.
Bolsius, nephridial cells, 47.
Bonnet, theory of development, 8, 432.
Born, chromosomes in *Triton*-egg, 338; gravitation-experiments, 386.
Boveri, centrosome, named, 51; a permanent organ, 51, 74; in fertilization, 192, 211, 215, 230; structure, 309; functions, 354; archoplasm, 69, 318; origin of mitotic figure, 74, 77, 319; varieties of *Ascaris*, 87; theory of mitosis, 101, 108; division of chromosomes, 112; origin of germ-cells, 147; fertilization of *Ascaris*, 182; of *Pterotrachea*, 184; of *Echinus*, 192; theory of fertilization, 190, 211; of parthenogenesis, 281; partial fertilization, 190, 194; reduction, 233; maturation in *Ascaris*, 238; tetrads, 238; centriole, 309; attraction-sphere, 324; egg-fragments, 353.
Braem, cell-division, 377.
Brandt, symbiosis, 53; regeneration in Protozoa, 342.

Brauer, bivalent chromosomes, 82; mitosis in rhizopod, 96; fission of chromatin-granules, 113; deutoplasm, 153; fertilization in *Branchipus*, 192; parthenogenesis in *Artemia*, 281; spermatogenesis in *Ascaris*, 255; intra-nuclear centrosome, 304.
Braus, 81.
Brogniard, pollen-tube, 218.
Brooks, heredity, 12; variation, 179.
Brown, Robert, cell-nucleus, 18; pollen-tube, 218.
Brücke, cell-organization, 289.
Von Brunn, spermatozoön, 141.
Bühler, astral systems, 318.
Bütschli, 6; protoplasm, 25, 36, 50; diffused nuclei, 40; artifacts, 42; asters, 48, 316; cell-membrane, 54; mitosis, 109, 110; centrosome in diatoms, 51; rejuvenescence, 178; polar bodies, 238.

Calberla, micropyle, 200.
Calkins, nuclei of flagellates, 40; mitosis in *Noctiluca*, 92; yolk-nucleus, 157; origin of middle-piece, 165; reduction, 253, 257.
Campbell, fertilization in plants, 216.
Carnoy, nucleus, 40; muscle-fibre, 48; centrosome, 110; amitosis, 115, 117; germ-nuclei, 184; asters, 305, 317.
Carnoy and Le Brun, nucleoli, 130; fertilization, 211; reduction, 263.
Castle, egg-axis, 379; fertilization, 193.
Chittenden, organic synthesis, 341.
Chmielewski, reduction in *Spirogyra*, 280.
Chun, amitosis, 117; partial development of ctenophores, 418.
Clapp, first cleavage-plane, 381.
Coe, fertilization, 194, 213; centrosome, 321.
Cohn, cell, 17.
Conklin, size of nuclei, 71; union of germ-nuclei, 204; centrosome in fertilization, 210; centrosome and sphere, 323; unequal division, 373; protoplasmic currents, 377; cell-size and body-size, 388; types of cleavage, 423.
Corda, pollen-tube, 218.
Crampton, yolk-nucleus, 158; reversal of cleavage, 368; experiments on snail, 419, 421; on tunicates, 419.
Crato, protoplasm, 50.

Darwin, evolution, 2, 5; inheritance, 12, 396; variation, 11; pangenesis, 12, 290; gemmules, 290.
Darwin, F., protoplasmic fragments, 346.
Dendy, cell-bridges, 60.
Dogiel, amitosis, 118.
Driesch, dispermy, 198; fertilization of egg-fragments, 200, 353; pressure-experiments, 375, 410; regeneration, 393; isolated blastomeres, 409; theory of development, 394, 415; experiments on ctenophores, 418; ferment-theory, 427.
Drüner, spindle-fibres, 79; central spindle, 105; aster, 321, 326.

Von Ebner, Sertoli-cells, 284.
Ehrlich, tar-colours, 335.
Eismond, structure of aster, 48.
Elssberg, plastidules, 291.
Endres, experiments on frog's egg, 399, 419.
Engelmann, ciliated cells, 44; rejuvenescence, 179.
Von Erlanger, asters, 48, 316; spindle, 81; elimination of chromatin, 155; Nebenkern, 163, 165; fertilization, 194, 212, 213; centroplasm, 324.
Eycleshymer, first cleavage-plane, 381.

Farmer, reduction in plants, 275.
Fick, fertilization of axolotl, 192, 212.
Field, staining-reactions, 176.
Fischel, ctenophores, 419.
Fischer, nucleus, 40; artifacts, 42; staining-reactions, 335.
Flemming, protoplasm, 25, 27; chromatin, 33; centrosome, 51; cell-bridges, 60, 61; cell-division, 64, 70; splitting of chromosomes, 70; mitotic figure, 79; heterotypical mitosis, 86; leucocytes, 102; theory of mitosis, 106; division of chromatin, 113; amitosis, 117, 285; nucleoli, 127; rotation of sperm-head, 188; spermatogenesis, 259–262; astral rays, 317; germinal localization, 399.
Floderus, follicle-cells, 150.
Fol, 1, 6, 64; amphiaster, 68; theory of mitosis, 108; sperm-centrosome, 191; polyspermy, 192; attraction-cone, 198; vitelline membrane, 199; asters, 316.
Foot, yolk-nucleus and polar rings, 156, 202; fertilization in earthworm, 187; entrance-funnel, 201; fertilization-centrosome, 212.
Foster, cell-organization, somacules, 291.
Francotte, polar bodies, 235; centrosome, 306; sphere, 312, 325.
Frommann, protoplasm, 23; nucleus and cytoplasm, 303.

Galeotti, pathological mitoses, 97.
Gallardo, mitosis, 109.

Galton, inheritance, 9.
Gardiner, cell-bridges, 59; chromatin-elimination, 276; sphere, 325.
Garnault, fertilization in *Arion*, 207.
Geddes and Thompson, theory of sex, 124.
Van Gehuchten, spireme-nuclei, 36; nuclear polarity, 36; muscle-fibre, 48.
Giard, polar bodies, 235, 238.
Gierke, staining-reactions, 335.
Gilson, spireme-nuclei, 36.
Godlewski, spermatogenesis, 168.
Graf, nephridial cells, 47.
Grégoire, reduction, 267.
Griffin, fertilization, centrosomes in *Thalassema*, 193, 194, 213; reduction, 259; structure of centrosome, 314; aster-formation, 321.
Grobben, spermatozoa, 141.
Gruber, diffused nuclei, 40; regeneration in *Stentor*, 342.
Guignard, mitosis in plants, 82; fertilization in plants, 218, 221; reduction, 263, 267.

Haberlandt, position of nuclei, 346.
Häckel, inheritance, 7; epithelium, 56; cell-state, 58.
Häcker, polar spindles, 276; bivalent chromosomes, 88; nucleolus, 125, 128; primordial germ-cells, 148; germ-nuclei, 208, 299; reduction in copepods, 249.
Hallez, promorphology of ovum, 384.
Halliburton, proteids, 331; nuclein, 333.
Hamm, discovery of spermatozoön, 9, 181.
Hammar, cell-bridges, 60.
Hammarsten, proteids, 331.
Hansemann, pathological mitoses, 97.
Hanstein, metaplasm, 19.
Hardy, artifacts, 42.
Harper, mitosis, 82.
Hartsoeker, spermatozoön, 9.
Harvey, inheritance, 7; epigenesis, 8.
Hatschek, cell-polarity, 56; fertilization, 179.
Heidenhain, nucleus, 36; basichromatin and oxychromatin, 38, 337; cell-polarity, 55; position of centrosome, 57; leucocytes, 102; theory of mitosis, 105; amitosis, 116; staining-reactions, 337; nuclear microsomes, 303; microcentrum, 311; asters, 311, 317; origin of centrosome, 315; position of spindle, 377.
Heider, insect-egg, 132.
Heitzmann, cell-bridges, 59; nucleus and cytoplasm, 303.
Henking, fertilization, 187; insect-egg, 96; spermatogenesis, 165, 248, 253, 271.
Henle, granules, 289.
Henneguy, deutoplasm, 153; yolk-nucleus, 160; centrosome, 356.
Hensen, rejuvenescence, 179.
Herbst, development and environment, 428.
Herla, independence of chromosomes, 208, 299.
Hermann, central spindle, 78, 105; division of chromatin, 112; spermatozoön, 165, 166; staining-reactions, 176.
Hertwig, O., 1, 7, 9; bivalent chromosomes, 88; pathological mitoses, 97; rejuvenescence, 178; fertilization, 181; middle-piece, 187; polyspermy, 199; paths of germ-nuclei, 204; maturation, 241; polar bodies, 238; inheritance, 182; laws of cell-division, 364; theory of development, 415.
Hertwig, O. and R., 197; egg-fragments, 199; polyspermy, 199.
Hertwig, R., mitosis in Protozoa, 90; germ-cells in *Sagitta*, 146; amphiasters in unfertilized eggs, 306; conjugation, 222; reduction in Infusoria, 277; in *Actinosphærium*, 278; origin of centrosome, 315; cell-division, 391.
Hill, fertilization, 187, 193.
Hirase, spermatozoids, 144; fertilization, 218.
His, germinal localization, 398.
Hofer, regeneration in *Amœba*, 343.
Hoffman, micropyle, 200.
Hofmeister, cell-division and growth, 393.
Holmes, cleavage, 368.
Hooke, R., cell, 17.
Hoyer, amitosis, 115.
Huie, *Drosera*, 350.
Huxley, protoplasm, 5; germ, 7, 396; fertilization, 178, 231; evolution and epigenesis, 432.

Ikeno, cell-bridges, 150; blepharoplasts, 173; fertilization, 221.
Ishikawa, *Noctiluca*, mitosis, 92; conjugation, 227; reduction, 267; flagellum, 171.

Jennings, cleavage, 377.
Jordan, deutoplasm and yolk-nucleus, 153, 156; first cleavage-plane, 381.
Julin, fertilization in *Styleopsis*, 192.

Keuten, mitosis in *Euglena*, 91.
Klebahn, conjugation and reduction in desmids and diatoms, 280.

Klebs, pathological mitosis, 97, 98; cell-membrane, 346.

Klein, nuclear membrane, 38; theory of mitosis, 100; amitosis, 118; nucleus and cytoplasm, 303; asters, 316.

Klinckowström, fertilization, 213; reduction, 259.

Von Kölliker, 1, 6, 9, 10, 27; epithelium, 56; cell-division, 63; spermatozoön, 9, 134; inheritance, 182; development, 413.

Korff, spermatogenesis, 163, 168, 173.

Korschelt, nucleus, 37; amitosis, 115; movements and position of nuclei, 125, 349, 387; nurse-cells, 151; fertilization, 193; tetrads in *Ophryotrocha*, 258; physiology of nucleus, 348; polarity of egg, 387.

Kossel, chromatin, 336; nuclein, 334; organic synthesis, 340.

Kostanecki, fertilization, 193; astral rays, 318.

Kostanecki and Wierzejski, fertilization of *Physa*, 193, 210, 212; continuity of centrosomes, 211.

Kupffer, energids, 30; cytoplasm, 41.

Lamarck, inheritance, 12.

Lamarle, minimal contact-areas, 361.

Lankester, germinal localization, 398.

Lauterborn, mitosis in diatoms, 95; origin of centrosome, 315.

Leeuwenhoek, spermatozoön, 8; fertilization, 181.

Von Lenhossék, nerve-cell, 21, 47; spermatogenesis, 169, 315; centrosome, 314, 356.

Leydig, cell, 19; protoplasm, 20; cell-membrane, 54; spermatozoa, 142; elimination of chromatin, 159.

Lilienfeld, staining-reactions of nucleins, 336.

Lillie, fertilization, 196, 213; centrosome and aster, 312, 326, 327; regeneration in *Stentor*, 343; cleavage, 360, 369, 377.

Loeb, chemical fertilization, 215, 392; regeneration in cœlenterates, 392; theory of development, 427; environment and development, 430.

Lustig and Galeotti, pathological mitoses, 98; centrosome, 51.

Maggi, granules, 290.

Malfatti, staining-reactions of nucleins, 335.

Mark, germ-nuclei, 204; polar bodies, 235; polarity of ovum, 387.

Mathews, pancreas-cell, 44; aster-formation, 110; fertilization of echinoderms, 192, 212; origin of centrosome, 125; nucleic acid, 334; staining-reactions, 337.

Maupas, sex in Rotifers, 145; rejuvenescence, 179; conjugation of Infusoria, 223.

Mayer, staining, 335.

McClung, spermatogenesis, 271.

MacFarland, spindle, 79; fertilization, 213, 214; centrosome and sphere, 312, 314, 321.

McGregor, spermatogenesis, 167; reduction, 261.

McMurrich, gasteropod development, 152; metamerism in isopods, 390.

Mead, fertilization of *Chætopterus*, 192, 194, 215; sperm-centrosome, 215; centrosomes *de novo*, 212, 306; cell-division, 391.

Merkel, Sertoli-cells, 284.

Mertens, yolk-nucleus and attraction-sphere, 156, 159.

Metschnikoff, insect-egg, 383.

Meves, amitosis, 119, 285; spermatogenesis, 167, 169; reduction, 260; cilia, 357.

Meyer, energids, 30; cell-bridges, 60.

Miescher, nuclein, 332.

Mikosch, protoplasm, 44.

Minot, rejuvenescence, 179; cyclical division, 222; theory of sex, 243; Sertoli-cells, 284; parthenogen sis, 280.

Von Mohl, cell-division, 9; protoplasm, 17.

Montgomery, nucleolus, 34; spermatogenesis, 257, 271.

Moore, spermatozoön, 167, 171; reduction, 263.

Morgan, centrosomes, 307; fertilization of egg-fragments, 353; cell-division, 391; effect of fertilization, 201; numerical relations of cells, 389; regeneration, 393, 394; isolated blastomeres, 410; polarity, 417; experiments on ctenophores, 418; on frog's egg, 422.

Mottier, mitosis, 83; fertilization, 221; reduction, 266; asters, 305.

Munson, yolk-nucleus, 156.

Nägeli, development, 1; cell-organization, micellæ, 289, 291; polioplasm, 41; idioplasm-theory, 401.

Nawaschin, fertilization, 218.

Nemec, mitosis, 82; yolk-nucleus, 159.

Newport, fertilization, 181; first cleavage-plane, 380.

Nissl, chromophilic granules, 48.

Nussbaum, germ-cells, 122; sex, 145; regeneration in Infusoria, 342; nucleus, 426.

Obst, nucleoli, 130; follicle-cells, 151.

Osterhout, spindle, 82; tetrads, 253.

Overton, germ-cells of *Volvox*, 134; conjugation of *Spirogyra*, 229; reduction, 274, 275.
Owen, germ-cells, 122.

Paladino, cell-bridges, 60.
Paulmier, spermatozoön, 165; reduction, 252, 271.
Peremeschko, leucocytes, 117.
Peter, cilia, 357.
Pfeffer, hyaloplasm, 41; amitosis, 119; chemotaxis of germ-cells, 197.
Pfitzner, cell-bridges, 60; chromatin-granules, 112.
Pflüger, position of spindle, 375; first cleavage-plane, 380; gravitation-experiments, 386; isotropy, 378.
Plateau, minimal contact-areas, 366.
Platner, mitosis, 110; egg-centrosome, 125; formation of spermatozoön, 163; fertilization of *Arion*, 207; maturation, 241.
Pouchet and Chabry, development and environment, 428.
Prenant, spermatozoön, 162; archoplasm, 322.
Preusse, amitosis, 119.
Prévost and Dumas, cleavage, 10.
Pringsheim, Hautschicht, 41; fertilization, 181.
Purkinje, protoplasm, 17.

Rabl, nuclear polarity, 36; cell-polarity, 56; centrosome in fertilization, 210; individuality of chromosomes, 294; astral systems, 317.
Ranvier, blood-corpuscles, 54.
Vom Rath, bivalent chromosomes, 88; amitosis, 118, 225; early germ-cells, 149; reduction, 249.
Rauber, cell-division and growth, 393.
Rawitz, amitosis, 116; staining-reactions, 335.
Redi, genetic continuity, 290.
Reichert, cleavage, 10, 64.
Reinke, pseudo-alveolar structure, 50; nucleus, 38, 303; œdematin, 36; asters, 305; nucleus and cytoplasm, 303.
Remak, cleavage, 1, 10, 361; cell-division, 64; egg-axis, 378.
Retzius, muscle-fibre, 48; cell-bridges, 60; end-piece, 140.
Rhumbler, 105.
Robin, germinal vesicle, 64.
Rosen, staining-reactions, 220.
Roux, 245, 301, 351; meaning of mitosis, 244, 301, 351, 405; position of spindle, 377; first cleavage-plane, 380; frog-experiments, mosaic theory, 399; theory of development, 405; post-generation, 408.
Rückert, pseudo-reduction, 248; fertilization of *Cyclops*, 193; independence of germ-nuclei, 208, 209; reduction in copepods, 249, 251; early history of germ-nuclei, 273; reduction in selachians, 257; history of germinal vesicle, 338.
Rüge, amitosis, 117.
Ryder, staining-reactions, 175.

Sabaschnikoff, tetrads, 256.
Sabatier, amitosis, 116.
Sachs, energid, 19, 30; laws of cell-division, 362; cell-division and growth, 393; development, 427.
St. George, La Valette, spermatozoön, 10, 134; spermatogenesis (terminology), 161.
Sala, polyspermy, 199.
Sargant, reduction in plants, 267.
Schäfer, protoplasm, 29.
Scharff, budding of nucleus, 155.
Schaudinn, mitosis in *Protozoa*, 92, 94, 102; polar bodies, 278.
Schewiakoff, mitosis in *Euglypha*, 91.
Schimper, plastids, 290.
Schleicher, karyokinesis, 64.
Schleiden, cell-theory, 1; cell-division, 9; nature of cells, 17; fertilization, 218.
Schloter, granules, 38, 303.
Schmitz, plastids, 290; conjugation, 216.
Schneider, discovery of mitosis, 64.
Schottländer, multipolar mitosis, 99.
Schultze, M., cells, 1, 19; protoplasm, 20.
Schultze, O., mitosis, 318; gravitation-experiments, 422; double embryos, 422.
Schwann, cell-theory, 1; the egg a cell, 8; origin of cells, 9; nature of cells, 17; organization, 58; adaptation, 433.
Schwarz, protoplasm, 42; linin, 33; chemistry of nucleus, 41; nuclei of growing cells, 340.
Schweigger-Seidel, spermatozoön, 9, 134.
Sedgwick, cell-bridges, 60.
Seeliger, egg-fragments, 353; egg-axis, 379.
Selenka, double spermatozoa, 142.
Shaw, spermatozoids, 175.
Siedlecki, polar bodies, 280.
Sobotta, fertilization, 185, 211.
Solger, pigment-cells, 102; attraction-sphere, 51.
Spallanzani, spermatozoa, 9; regeneration, 393.

Spencer, physiological units, 289; development, 432.
Stauffacher, egg-centrosome, 125.
Stevens, fertilization, 217.
Strasburger, 1, 7; cytoplasm, 20; Körnerplasma, 41; centrosphere, 68, 356, 324; membranes, 55; origin of amphiaster, 82; multipolar mitoses, 99; theory of mitosis, 105, 110; spermatozoids, 173; kinoplasm, 27, 82, 322; staining-reactions of germ-nuclei, 220; fertilization in plants, 216, 219, 221; reduction, 265, 269; theory of maturation, 275; organization, 289; inheritance, 7, 182, 351; action of nucleus, 426.
Zur Strassen, giant-embryos, 296; germ-cells, 148.
Van der Stricht, spindle, 79; amitosis, 116; fertilization, 210; reduction, 259; centrosome and sphere, 312, 325.
Ströbe, multipolar mitoses, 99.
Stuhlmann, yolk-nucleus, 156.
Suzuki, spermatogenesis, 168.
Swingle, mitosis, 82.

Tangl, cell-bridges, 59.
Thiersch and Boll, theory of growth, 392.
Townsend, cell-bridges, 61, 346.
Treat, sex, 145.
Treviranus, variation, 179.

Unna, protoplasm, 27.
Ussow, micropyle, 133; deutoplasm, 153.

Vejdovský, centrosome, 76; fertilization in *Rhynchelmis*, 192, 194; metamerism in annelids, 390.
Verworn, cell-physiology, 6; regeneration in *Protozoa*, 344; inheritance, 359, 431.
Virchow, 1; cell-division, 10, 63; protoplasm, 25; cell-state, 58.
De Vries, organization, pangens, 291, 327, 406; tonoplasts, 53; plastids, 229; chromatin, 431; development, 404.

Waldeyer, nucleus, 38; cytoplasm, 41; cell-membrane, 54.
Walter, frog-experiments, 419.
Watasé, theory of mitosis, 106; staining-reactions of germ-nuclei, 176; nucleus and cytoplasm, 292; asters, 305; theory of centrosome, 315; astral rays, 321; cleavage of squid, 381; promorphology of ovum, 383, 386.
Webber, spermatozoids, 144, 173; fertilization, 221.
Weismann, inheritance, 12; cell-organization, biophores, 291; somatic and germ cells, 122; amphimixis, 179; maturation, 243–246; constitution of the germ-plasm, 245; parthenogenesis, 281; theory of development, 404, 407, 432.
Went, vacuoles, 53.
Wheeler, amitosis, 115; insect-egg, 132; egg of *Myzostoma*, 151; fertilization in *Myzostoma*, 208; bilaterality of ovum, 383.
Whitman, on Harvey, 7; polar rings, 202; cell-division and growth, 393; polarity, 384; theory of development, 400, 416.
Wiesner, cell-organization, 290, 291.
Wilcox, sperm-centrosome, 165; reduction, 257.
Will, chromatin-elimination, 135.
Wilson, protoplasm, 27, 44; mitosis, 106; fertilization in sea-urchin, 187, 212; paths of germ-nuclei, 202; origin of linin, 303; astral rays, 28; centrosphere and centrosome, 314; dispermy, 355; rudimentary cells, 372; pressure-experiments, 411; experiments on *Amphioxus*, 410; theory of development, 415.
Von Wittich, yolk-nucleus, 155.
Wolff, C. F., epigenesis, 8.
Wolff, G., regeneration of lens, 433.
Wolters, polar bodies in gregarines, 278.

Yung, sex, 144.

Zacharias, E., nucleoli, 34; of meristem, 37; staining-reactions, 176; nuclein in growing-cells, 340.
Zacharias, O., amœboid spermatozoa, 142.
Ziegler, artificial mitotic figure, 108; amitosis, 117; sphere, 324.
Zimmerman, pigment-cells, 102; centrosome, 356.
Zoja, independence of chromosomes, 299; isolated blastomeres, 410.

INDEX OF SUBJECTS

Acanthocystis, 94, 304, 306.

Achromatic figure (see Amphiaster), 69; varieties of, 78; nature, 316.

Achromatium, 39.

Actinophrys, 92, 278.

Actinosphærium, mitosis, 90, 94; reduction, 278; regeneration, 342.

Æquorea, metanucleus, 128.

Albugo, 217.

Albumin, 331.

Allium, 83, 253, 267.

Allolobophora, teloblasts, 374.

Alveoli, 25.

Amitosis, 114; biological significance, 116; in sex-cells, 285.

Amœba, 5; mitosis, 91; experiments on, 343.

Amphiaster, 68; asymmetry of, 70, 373; origin, 72, 74, 316; in amitosis, 116; in fertilization, 187, 213; nature, 316; position, 375.

Amphibia, spermatozoa, 140; sex, 145.

Amphioxus, fertilization, 210; polar body, 236, 277; cleavage, 370; dwarf larvæ, 389, 410; double embryos, 410.

Amphipyrenin, 41.

Amphiuma, 167, 261.

Amyloplasts, 53; in plant-ovum, 133.

Anaphases, 70; in sea-urchin egg, 106.

Anasa, sperm-formation, 165, 271; reduction, 272.

Ancylus, 368.

Anilocra, gland-cells, nuclei, 36; amitosis, 116.

Anodonta, ciliated cells, 43, 357.

Antipodal cone, 101.

Aphis, 281.

Arbacia, 192, 215, 307.

Archoplasm, 69; in developing spermatozoa, 171; nature of, 318.

Archosome, 52.

Argonauta, micropyle, 133.

Aricia, rudimentary cells, 372.

Arion, spindle, 81; germ-nuclei, 207.

Arisæma, 269.

Artemia, chromosomes, 89; parthenogenetic maturation, 281.

Artifacts, in protoplasm, 42.

Ascaris, chromosomes, 87, 301; mitosis, 80, 101; primordial germ-cells, 146; fertilization, 182, 211; polyspermy, 199; polar bodies, 238; spermatogenesis, 241, 253; individuality of chromosomes, 295; intranuclear centrosome, 304; centrosome, 311; attraction-sphere, 323; supernumerary centrosome, 355.

Aster, 68; asymmetry, 70; structure and functions, 101; in amitosis, 116; in fertilization, 187, 213; nature of, 316; finer structure, 326; relative size, 70, 373.

Asterias, spermatozoa, 176; sperm-aster, 187; fertilization, 192, 210.

Astrocentre, 324.

Astrosphere, 324.

Attraction-cone, 198.

Attraction-sphere, 51, 72; in amitosis, 115; of the ovum, 125; of the spermatid, 163; in resting cells, 323; nature of, 323.

Axial filament, 136; origin of, 165.

Axis, of the cell, 55; of the nucleus, 36, 294; of the ovum, 378, 386.

Axolotl, fertilization, 192.

Bacteria, nuclei, 31, 39.

Basichromatin, 38; staining-reactions, 338.

Bioblast, 290.

Biogen, 291.

Biophore, 245, 291.

Birds, blood-cells, 57; spermatozoa, 138; young ova, 155.

Blastomeres, displacement of, 366; individual history, 378; prospective value, 415; rhythm of division, 366, 389; development of single, 409, 418; in normal development, 423.

Blennius, pigment-cells, 103.

Blepharoplastoids, 175.

Blepharoplasts, 173, 221.

Branchipus, yolk, 153; sperm-aster, 192; reduction, 256.

Calanus, tetrads, 250.

Caloptenus, 165, 257.

Cambium, 376.

Cancer-cells, mitosis, 98.

Canthocamptus, reduction, 251; ovarian eggs, 273.

Cell, in general, 4; origin, 9; name, 17; general sketch, 19; polarity of, 55; as a structural unit, 58; structural basis, 23, 293; physiology and chemistry, 330; size and numerical relations, 389; in inheritance, 9, 430; differentiation of, 413, 426; independence of, 427.

Cell-bridges, 59.

Cell-division (see Mitosis, Amitosis), general significance, 10, 63; general account, 65; types, 64; Remak's scheme, 63; indirect, 65; direct, 114; cyclical character, 178, 223; equal and reducing or qualitative, 405; relation to development, 388, 405, 410, 427; Sachs's laws, 362; rhythm, 366, 389; unequal, 370; of teloblasts, 371; energy of, 388; relation to metamerism, 390; causes, 391; relation to growth, 388; and differentiation, 427.

Cell-membrane, 53.

Cell-organization, 289.

Cell-organs, 52; nature of, 291; temporary and permanent, 292.

Cell-plate, 71.

Cell-state, 58.

Cell-theory, general sketch, 1–14.

Central spindle, 70, 78.

Centrodesmus, 79, 315.

Centrodeutoplasm, 163, 324.

Centroplasm, 324.

Centrosome, 22; general sketch, 50, 304; position, 55; in mitosis, 74; a permanent organ, 74; dynamic centre, 76; historical origin, 315; functions, 101, 354; in amitosis, 115; of the ovum, 125; of the spermatozoön, 137, 165–170; in fertilization, 190, 208; degeneration of, 186, 213; continuity, 74, 77, 194, 214, 321; nature, 304; intra-nuclear, 304; supernumerary, 355.

Centrosphere, 68, 85; nature of, 324.

Ceratium, 91.

Ceratozamia, reduction, 275.

Cerebratulus, 193, 194, 213, 306, 307, 321, 325.

Cerianthus, regeneration in, 392.

Chætopterus, spindle, 81, 84; fertilization, 192; sperm-centrosome, 213; centrosomes *de novo*, 306; cell-division, 391.

Chara, spermatozoids, 143.

Chilomonas, 32, 40, 192.

Chironomus, spireme-nuclei, 36.

Chorion, 132.

Chromatic figure, 69; origin, 72; varieties, 86; in fertilization, 181, 204.

Chromatin, 33; in meristem, 37; in mitosis, 65, 86; in cancer-cells, 98; of the egg-nucleus, 126; elimination of, in cleavage, 147, 426; in oögenesis, 233, 276; staining-reactions, 334–340; morphological organization, 37, 245, 294; chemical nature, 332, 404; relations to linin, 302; physiological changes, 338; as the idioplasm, 352; in development, 405, 425, 431.

Chromatin-granules, 37; in mitosis, 112; in reduction, 248; general significance, 301–304; relations to linin, 302.

Chromatophore, 53; in the ovum, 133; in fertilization, 229.

Chromiole, 302.

Chromomere (see Chromatin-granule), 37, 301.

Chromoplast, 53.

Chromosomes, 67, 70, 86, 112; number of, 67, 206; bivalent and plurivalent, 87; division, 112; of the primordial germ-cell, 148; in fertilization, 182, 204; independence in fertilization, 204; reduction, 238, 243, 248; in early germ-nuclei, 273; conjugation of, 257; in parthenogenesis, 281; individuality of, 294; composition of, 301; chemistry, 334, 336; history in germinal vesicle, 338; in dwarf larvæ, 296.

Ciliated cells, 44, 57.

Ciona, egg-axis, 379.

Clavelina, cleavage, 369, 381.

Cleavage, in general, 10; geometrical relations, 362; Sachs's rules, 362; Hertwig's rules, 364; modifications of, 366; spiral, 368; reversal of, 368; unequal, 370; under pressure, 375, 411; promorphology of, 378; bilateral, 381; rhythm, 366, 388; mosaic theory, 399, 423; half cleavage, 410.

Cleavage-nucleus, 204.

Cleavage-planes, 362; axial relations, 378.

Clepsine, nephridial cell, 45; polar rings, 202; cleavage, 370.

Closterium, conjugation and reduction, 280.

Cockroach, amitosis, 115; orientation of egg, 384.

Cœlenterates, germ-cells, 146; regeneration, 392, 393, 430.

Conjugation, in unicellular animals, 222; unicellular plants, 228, 280; physiological meaning, 178, 223.

Contractility, theory of mitosis, 100; inadequacy, 106.
Copepods, reduction, 251.
Corixa, ovum, 383.
Corpuscule central, 310, 314.
Crepidula, fertilization, 210; dwarfs and giants, 389; cleavage, 323, 423.
Cross-furrow, 368.
Crustacea, spermatozoa, 142.
Ctenophores, experiments on eggs, 418.
Cucurbita, 346.
Cuticular, 54.
Cyanophyceæ, nucleus, 31, 39.
Cycads, spermatozoids, 144, 173; fertilization, 218, 221.
Cyclops, ova, 128; primordial germ-cells, 148; fertilization, 188; reduction, 251; attraction-sphere, 325; axial relations, 385.
Cytoplasm, 21, 41, 293, 303; of the ovum, 130; of the spermatozoön, 134; morphological relations to nucleus, 302; to archoplasm, 316, 319; chemical relations to nucleus, 333–341; physiological relations to nucleus, 341; in inheritance, 352–354, 359; in development, 398, 421; origin, 431.
Cytosome, 322.

Dendrobæna, metamerism, 390.
Determinants, 245.
Deutoplasm, 131; deposit, 153; effect on cleavage, 366, 371; rearrangement by gravity, 422.
Development, 1–12; and cell-division, 388; mosaic theory, 399, 421; theory of Nägeli, 402; Roux-Weismann theory, 404; of single blastomeres, 399, 409, 418; of egg-fragments, 296, 353, 419; De Vries's theory, 413; Hertwig's theory, 415, 432; Driesch's theory, 394, 415; partial, 409, 419; half and whole, 419; nature of, 413; external conditions, 428; and metabolism, 430; unknown factor, 431; rhythm, 432; adaptive character, 433.
Diaptomus, 250.
Diatoms, mitosis, 92; centrosome, 51.
Diaulula, 79, 314.
Diemyctylus, yolk, 153; yolk-nuclei, 156.
Differentiation, 361; theory of De Vries, 404; of Weismann, 405; nature and causes, 413; of the nuclear substance, 425; and cell-division, 427.
Dipsacus, 346.
Dispermy, 355.
Double embryos, 410, 422.
Drosera, 350.
Dwarfs, formation of, 353, 410, 422; size of cells, 389.
Dyads (Zweiergruppen), 239, 241; in parthenogenesis, 284.
Dyaster, 70.
Dycyemids, centrosome, 51.
Dytiscus, ovarian eggs, 153, 349.

Earthworm, ova, 152; spermatozoön, 165; yolk-nucleus, 154; polar rings, 156, 202; spermatogenesis, 257; teloblasts, 374.
Echinoderms, protoplasm, 28, 44, 293; spermatozoa, 137; fertilization, 188, 212; polyspermy, 194, 198; dwarf larvæ, 353, 410; half cleavage, 410; eggs under pressure, 411; modified larvæ, 428.
Echinus, fertilization, 210; centrosome, 314; dwarf larvæ, 353; number of cells, 389.
Ectosphere, 324.
Egg-axis, 378; promorphological significance, 379; determination, 386; alteration of, 422.
Egg-fragments, fertilization, 194; development, 352.
Elasmobranchs, spermatozoön, 140, 167, 169; germinal vesicle, 245, 273; reduction, 257.
Embryo-sac, 218, 263.
Enchylema, 23.
End-knob, 136.
Endoplasm, 41.
End-piece, 140.
End-plate, 91.
Energid, 19, 30.
Entosphere, 324.
Envelopes, of the egg, 132.
Epigenesis, 8, 432.
Equatorial plate, 68.
Equisetum, mitosis, 85.
Ergastoplasm, 322.
Erysiphe, mitosis, 82.
Euchæta, tetrads, 250.
Euglena, mitosis, 91, 315.
Euglypha, mitosis, 89, 95.
Evolution (preformation), 8, 399, 432.
Evolution, theory of, 2, 8.
Exoplasm, 41.

Fertilization, general aspect, 9; physiological meaning, 180; general sketch, 180; *Ascaris*, 182; mouse, 185; sea-urchin, 188; *Nereis*, 188; *Cyclops*, 188; *Thalassema*, *Chætopterus*, 193, 195; pathological, 198; partial, 190, 194; of *Myzostoma*, 196, 208; in plants, 215; egg-fragments, 194; Boveri's theory, 192, 211.

Fishes, pigment-cells, 102; periblast-nuclei, 117; spermatozoa, 137; young ova, 116; single blastomeres, 410.
Flagellates, diffused nuclei, 39.
Follicle, of the egg, 150.
Forficula, nurse-cells, 151.
Fragmentation, 64.
Fritillaria, spireme, 112; fertilization, 219.
Frog, tetrads, 259; egg-axis, 378; first cleavage-plane, 380; Roux's puncture experiment, 399; post-generation, 409; pressure-experiments, 410; effect of gravity on the egg, 422; development of single blastomeres, 399, 408, 422; double embryos, 422.
Fucus, 143, 217, 221.

Ganglion-cell, 48; centrosome in, 51, 314.
Gemmæ, 291.
Gemmules, 12, 291.
Genoblasts, 243.
Geophilus, deutoplasm, 154, 158; yolk-nucleus, 156.
Germ, 7, 396.
Germ-cells, general, 8, 9; detailed account, 122; of plants, 133, 142; origin, 144; growth and differentiation, 150; union, 196; results of union, 200; maturation, 233; early history of nuclei, 272.
Germinal localization, theory of, 397.
Germinal spot, 124.
Germinal vesicle, 124, 125; early history, 273; movements, 349; position, 387.
Germ-nuclei, of the ovum, 125; of the spermatozoön, 135; of plants, 216; staining-reactions, 175; in fertilization, 182, 188; equivalence, 182, 205; paths, 202; movements, 204; union, 204; independence, 204, 299; in Infusoria, 224; early history, 272.
Giant-cells, 31; microcentrum, 314.
Gingko, 173.
Globulin, 331, 333.
Granules (see Microsomes), of Altmann, 290; nuclear, 37, 303; chromophilic, 23, 48; in general, 289.
Gravity, effect on the egg, 131, 422.
Gregarines, mitosis, 89; polar body, 278.
Ground-substance, of protoplasm, 23; of nucleus, 36.
Growth, and cell-division, 58, 388.
Gryllotalpa, reduction, 249.
Guinea-pig, spermatogenesis, 170; maturation, 277.

Heliozoa, 92, 103.
Helix, 163, 168, 259.
Hemerocallis, 306.
Heterocope, tetrads, 250.
Heterokinesis, 406.
Histon, 334, 336.
Homœokinesis, 406.
Hydrophilus, orientation of egg, 384.

Id, in reduction, 245; in inheritance, 406.
Idant, 245.
Idioblast, 291.
Idioplasm, theory of, 401; as chromatin, 403; action of, 406, 414, 431, 432.
Idiosome, 291.
Idiozome, 163, 165, 324.
Ilyanassa, partial development, 419.
Infusoria, nuclei, 31, 224; mitosis, 90; conjugation, 223; reduction, 277.
Inheritance, of acquired characters, 12, 433; Weismann's theory, 12; through the nucleus, 351–354; and metabolism, 430.
Inotagmata, 291.
Insect-eggs, 132, 386.
Interzonal fibres, 70.
Iris, 267.
Isopods, metamerism, 390.
Isotropy, of the egg, 384, 417.

Karyokinesis (see Mitosis), 64.
Karyokinetic figure (see Mitotic Figure), 69.
Karyolymph, 36.
Karyoplasm, 21.
Karyosome, 34.
Kinoplasm (archoplasm), 54, 77, 82, 173, 322.

Lanthanin, 38.
Lepidoptera, sex, 144.
Leucocytes, structure, 102; division, 117; centrosome, 309; attraction-sphere, 326.
Leucoplasts, of plant-ovum, 133.
Lilium, mitosis, 83; spireme, 112; fertilization, 219; reduction, 265–271.
Limax, germ-nuclei, 204.
Limulus, 158.
Linin, 32; relations to cytoreticulum and chromatin, 302.
Liparis, 281.
Locusta, orientation of egg, 384.
Loligo, spindle, 81; cleavage, 381.
Lumbricus, yolk-nucleus, 157; reduction, 257.

Macrobdella, 305.
Macrogamete, 226.
Macromeres, 371.
Mammals, spermatozoa, 139, 169; young ova, 155.
Mantle-fibres, 78, 105.
Marsilia, 175.
Maturation (see Reduction), 234; theoretical significance, 243; of parthenogenetic eggs, 280; nucleus in, 353.
Medusæ, dwarf embryos, 410.
Meristem, nuclei of, 340.
Metamerism, 390.
Metanucleus, 128.
Metaphase, 69.
Metaplasm, 19.
Micellæ, 291.
Microcentrum, 311, 315, 324.
Microgamete, 226.
Micromeres, 371.
Micropyle, 124, 133.
Microsomes, 23; of the egg-cytoplasm, 131; nature of, 289, 290, 293; of the astral systems, 318, 326; of the nucleus, 301, 303; relation to centrosome, 315; staining-reactions, 337.
Microsphere, 324.
Microzyma, 291.
Mid-body, 71, 78.
Middle-piece, 135, 139; origin, 161, 165–170; in fertilization, 187, 212.
Mitosis, 64; general outline, 65; modifications of, 77; heterotypical, 86; in unicellular forms, 87; pathological, 88; multipolar, 97; mechanism of, 100; physiological significance, 351; Roux-Weismann conception of, 245, 406.
Mitosome, 165.
Mitotic figure (see Mitosis, Spindle), 69; origin, 72; varieties, 78.
Molgula, 158.
Mouse, fertilization, 185, 193.
Musca, ovum, 142.
Myriapods, spermatozoa, 142; yolk-nucleus, 156.
Myzostoma, fertilization, 196, 208.

Naias, 266.
Nebenkern, pancreas-cells, 44; of spermatid, 163, 165.
Nebenkörper, 164, 165.
Necturus, pancreas-cells, 44.
Nematodes, germ-nuclei, 184.
Nereis, asters, 49; perivitelline layer, 131; ovum, 129; deutoplasm, 131; fertilization, 191; attraction-sphere and centrosome, 325; cleavage, 366, 369; pressure-experiments on, 411.
Nerve-cell, 48.
Net-knot, 34.
Noctiluca, mitosis, 93; flagellum, 171; conjugation, 227; sphere, 319.
Nuclear stains, 335.
Nuclein, 33, 332; staining-reactions, 334; physiological significance, 340.
Nuclein-bases, 331.
Nucleinic acid, 33, 332–334; staining-reactions, 334; physiological significance, 340.
Nucleo-albumin, 331, 334.
Nucleo-proteid, 331, 334.
Nucleolus, 33; in mitosis, 67; of the ovum, 126; physiological meaning, 128.
Nucleoplasm, 21.
Nucleus, general structure and functions, 31; finer structure, 37; polarity, 36, 294; chemistry, 41; in mitosis, 65; of the ovum, 125; of the spermatozoön, 135, 137; relation to cytoplasm, 302; morphological composition, 294; in organic synthesis, 340, 430; physiology, 341; position and movements, 346; in fertilization, 181, 352; in maturation, 353; in later development, 425; in metabolism and inheritance, 430; in inheritance and development, 341, 358, 405, 425, 431; control of the cell, 426.
Nurse-cells, 151.

Œdigonium, fertilization, 181; membrane, 346.
Onoclea, 175.
Oöcyte, 236.
Oögenesis, 234, 236.
Oögonium, 236.
Oösphere, 133.
Ophryotrocha, amitosis, 115; nurse-cells, 151; fertilization, 189, 193; tetrads, 258.
Opossum, spermatozoa, 142.
Organization, 289, 291; of the nucleus, 294, 301; of the egg, 397, 433.
Origin of species, 3.
Osmunda, reduction, 275.
Ovary, 123; of *Canthocamptus*, 273.
Ovum, in general, 8, 9; detailed account, 124; nucleus, 125; cytoplasm, 130; envelopes, 132; of plants, 133; origin and growth, 150; fertilization, 178; effects of spermatozoön upon, 201; maturation, 236; parthenogenetic, 280; promorphology, 378; bilaterality, 382.

Oxychromatin, 38, 303; staining-reactions, 337.
Oxydation-ferments, 351.
Oxytricha, 342.
Oyster, germ-nuclei, staining-reactions, 175.

Pallavicinia, reduction, 275.
Paludina, dimorphic spermatozoa, 141.
Pangenesis, 12, 290, 431.
Pangens, 291.
Parachromatin, 41.
Paralinin, 41.
Paramœba, mitosis, 94, 315.
Paramœcium, mitosis, 91; conjugation, 224; reduction, 277.
Paranucleus, 163.
Parthenogenesis, theories of, 281; polar bodies in, 280.
Pellicle, 54.
Pentatoma, 271.
Petromyzon, fertilization, 192, 212.
Phallusia, fertilization, 193, 212.
Physa, fertilization, 193, 210, 212; reversed cleavage, 368.
Physiological units, 289.
Pieris, spinning-gland, 37.
Pigment-cells, 102.
Pilularia, fertilization, 216.
Pinus, reduction, 275.
Planaria, regeneration, 394.
Plant-cells, plastids, 52; membranes, 54; mitosis, 82; cleavage-planes, 363.
Plasma-stains, 335.
Plasmocyte, 52.
Plasmosome, 34.
Plasome, 291.
Plastids, 52; of the ovum, 133; of the spermatozoid, 143; conjugation of, 229.
Plastidule, 291.
Plastin, 41, 331.
Pleurophyllidia, 78, 94.
Podophyllum, 267.
Polar bodies, 181; nature and mode of formation, 235–240; division, 236; in parthenogenesis, 281.
Polar rings, 156, 202.
Polarity, of the nucleus, 36; of the cell, 55; of the ovum, 378; determination of, 382.
Pole-plates, 91.
Pollen-grains, formation, 263–265.
Pollen-tube, 218.
Polyclades, cleavage, 416.
Polychœrus, 276, 325.
Polygordius, cleavage, 368.
Polyspermy, 198; prevention of, 199.
Polystomella, regeneration, 344.
Polyzonium, 159.
Porcellio, amitosis, 116.
Predelineation, 398.
Preformation (see Evolution).
Pressure, experiments, 375, 410.
Principal cone, 101.
Pristiurus, 338.
Promorphology (see Cleavage, Ovum).
Pronuclei, 202.
Prophase, 65.
Prosthecerœus, 213, 235, 256, 259, 306.
Prosthiostomum, 212.
Protamin, 334.
Proteids, 331.
Prothallium, 264; chromosomes in, 275.
Protoplasm, 4, 5, 17, 19; structure, 23, 42, 293; chemistry, 331.
Protoplast (see Plastid).
Pseudo-alveolar structure, 50.
Pseudo-reduction, 248.
Pteris, 253.
Pterotrachea, germ-nuclei, 186, 205.
Ptychoptera, spireme-nuclei, 35.
Pygæra, 165.
Pyrenin, 41.
Pyrenoid, 133.
Pyrrhocoris, 165, 248.

Quadrille of centres, 210.

Rat, spermatogenesis, 170.
Reduction, general outline, 234; parallel between the two sexes, 241; theoretical significance, 243; detailed account, 246; in plants, 263; Strasburger's theory of, 275; in unicellular forms, 277; by conjugation, 257; modes contrasted, 247.
Regeneration, Weismann's theory, 406; in frog-embryo, 409; nature of, 425, 427; in cœlenterates, 430; of lens, 433.
Rejuvenescence, 179, 224.
Renilla, ovum, 132.
Rhabdonema, amitosis, 115.
Rhynchelmis, fertilization, 192, 193, 212; cleavage, 370.
Rotifers, sex, 145.

Sagitta, number of chromosomes, 184; primordial germ-cells, 146; germ-nuclei, 184; spermaster, 191.
Salamander, epidermis, 3; spermatogonia, 20; mitosis in, 71, 78; pathological mitosis, 98; leucocytes, 102; spermatozoa, 140; maturation, 259.

Sargus, pigment-cells, 103.
Scyllium, 263.
Segmentation (see Cleavage).
Selaginella, spermatozoids, 197.
Senescence, 179.
Sepia, spindle, 81.
Sertoli-cells, 284.
Sex, 9; determination of, 144; Minot's theory of, 243.
Siphonophores, amitosis, 117.
Soma, 13.
Somacule, 291.
Somatic cells, 122; number of chromosomes, 233.
Spermary, 123.
Spermatid, 161, 163; development into spermatozoön, 164.
Spermatocyte, 161, 241.
Spermatogenesis (see Reduction), 234; general outline, parallel with oögenesis, 241.
Spermatogonium, 161, 241.
Spermatozeugma, 142.
Spermatozoid, structure and origin, 142, 172; in fertilization, 217, 221.
Spermatozoön, discovery, 9; structure, 134; essential parts, 135; giant, 141; double, 142; unusual forms, 142; of plants, 142; formation, 160; in fertilization, 181, 192; entrance into ovum, 197.
Sperm-centrosome, 135, 164–171; in fertilization, 192, 211–215, 221.
Sperm-nucleus, 135; origin, 164–171; in fertilization, 182, 190; rotation, 188; path in the egg, 202; in inheritance, 353; chemistry, 334.
Sphærechinus, fertilization, 193, 210; number of cells, 389; hybrids, 353; regeneration, 393.
Spindle (see Amphiaster, Central Spindle), 68; origin, 72, 79, 82; in Protozoa, 90; conjugation of, 227; nature of, 316; position, 375.
Spireme, 65.
Spirochona, mitosis, 90.
Spirogyra, nucleolus, 67; amitosis, 119; conjugation, 229; reduction, 280.
Spongioplasm, 25.
Spontaneous generation, 7.
Stem-cells, 148.
Stentor, regeneration, 342.
Stylonychia, senescence, 224.
Stypocaulon, mitosis, 82.
Surirella, 94.
Symbiosis, 53, 292.
Synapta, cleavage, 364.
Syncytium, 59.

Teloblasts, 371, 390.
Telophase, 71.
Tetrads (Vierergruppen), 238; origin, 246; in *Ascaris*, 241, 253; in arthropods, 248; ring-shaped, 248; in amphibia, 259; origin by conjugation, 257; formulas for, 247.
Tetramitus, 40, 92.
Thalassema, spindle, 81; fertilization, 193, 194, 213; reduction, 259, 263; centrosome, 321; attraction-sphere, 325.
Thalassicolla, experiments on, 344.
Thysanozoön, 212, 259, 326.
Tonoplast, 53.
Toxopneustes, cleavage, 10; mitosis, 107; ovum, 126; spermatozoön, 134; fertilization, 188; paths of germ-nuclei, 202; polar bodies, 114; double cleavage, 355.
Trachelocerca, diffused nuclei, 40.
Trillium, 269.
Triton, 140, 212, 263, 277.
Trophoplasm, 322, 401.
Tubularia, regeneration, 430.
Tunicates, egg-axis, 379; cleavage, 381.

Unicellular organisms, 5; mitosis, 88; conjugation, 222; reduction, 277; experiments on, 342.
Unio, centrosome and aster, 314; cleavage. 381.
Urostyla, 40.

Vacuole, 50, 53.
Vanessa, ovarian egg, 153.
Variations, 11; origin of, 433.
Vaucheria, membrane, 348.
Vitalism, 394, 417.
Vitelline membrane, 132; of egg-fragments, 132; formation of, 198; function, 199.
Volvox, germ-cells, 133.
Vorticella, conjugation, 226.

Xiphidium, 271.

Yellow cells (of Radiolaria), 53.
Yolk (see Deutoplasm), 152.
Yolk-nucleus, 155.
Yolk-plates, 131.

Zamia, 173, 221.
Zirphæa, 259, 263.
Zwischenkörper (mid-body), 71.
Zygnema, membrane, 346.
Zygospore, 228.

Columbia University Biological Series.

EDITED BY

HENRY FAIRFIELD OSBORN,
Da Costa Professor of Zoölogy in Columbia University,
AND
EDMUND B. WILSON,
Professor of Zoölogy in Columbia University.

This series is founded upon a course of popular University lectures given during the winter of 1892–3, in connection with the opening of the new department of Biology in Columbia College. The lectures are in a measure consecutive in character, illustrating phases in the discovery and application of the theory of Evolution. Thus the first course outlined the development of the Descent theory; the second, the application of this theory to the problem of the ancestry of the Vertebrates, largely based upon embryological data; the third, the application of the Descent theory to the interpretation of the structure and phylogeny of the Fishes or lowest Vertebrates, chiefly based upon comparative anatomy ; the fourth, upon the problems of individual development and Inheritance, chiefly based upon the structure and functions of the cell.

Since their original delivery the lectures have been carefully rewritten and illustrated so as to adapt them to the use of College and University students and of general readers. The volumes as at present arranged for include:

I. **From the Greeks to Darwin.** By Henry Fairfield Osborn.
II. **Amphioxus and the Ancestry of the Vertebrates.** By Arthur Willey.
III. **Fishes, Living and Fossil.** By Bashford Dean.
IV. **The Cell in Development and Inheritance.** By Edmund B. Wilson.
V. **The Foundations of Zoology.** By William Keith Brooks.

THE MACMILLAN COMPANY,
66 FIFTH AVENUE, NEW YORK.

I. FROM THE GREEKS TO DARWIN.

THE DEVELOPMENT OF THE EVOLUTION IDEA.

BY

HENRY FAIRFIELD OSBORN, Sc.D., PRINCETON,

Da Costa Professor of Zoölogy in Columbia University.

8vo. Cloth. $2.00, net.

This opening volume, "From the Greeks to Darwin," is an outline of the development from the earliest times of the idea of the origin of life by evolution. It brings together in a continuous treatment the progress of this idea from the Greek philosopher Thales (640 B.C.) to Darwin and Wallace. It is based partly upon critical studies of the original authorities, partly upon the studies of Zeller, Perrier, Quatrefages, Martin, and other writers less known to English readers.

This history differs from the outlines which have been previously published, in attempting to establish a complete continuity of thought in the growth of the various elements in the Evolution idea, and especially in the more critical and exact study of the pre-Darwinian writers, such as Buffon, Goethe, Erasmus Darwin, Treviranus, Lamarck, and St. Hilaire, about whose actual share in the establishment of the Evolution theory vague ideas are still current.

TABLE OF CONTENTS.

I. The Anticipation and Interpretation of Nature.
II. Among the Greeks.
III. The Theologians and Natural Philosophers.
IV. The Evolutionists of the Eighteenth Century.
V. From Lamarck to St. Hilaire.
VI. The First Half-century and Darwin.

In the opening chapter the elements and environment of the Evolution idea are discussed, and in the second chapter the remarkable parallelism between the growth of this idea in Greece and in modern times is pointed out. In the succeeding chapters the various periods of European thought on the subject are covered, concluding with the first half of the present century, especially with the development of the Evolution idea in the mind of Darwin.

II. AMPHIOXUS AND THE ANCESTRY OF THE VERTEBRATES.

BY

ARTHUR WILLEY, B.Sc. Lond.,

Tutor in Biology, Columbia University; Balfour Student of the University of Cambridge.

8vo. Cloth. $2.50, net.

The purpose of this volume is to consider the problem of the ancestry of the Vertebrates from the standpoint of the anatomy and development of Amphioxus and other members of the group Protochordata. The work opens with an Introduction, in which is given a brief historical sketch of the speculations of the celebrated anatomists and embryologists, from Étienne Geoffroy St. Hilaire down to our own day, upon this problem. The remainder of the first and the whole of the second chapter is devoted to a detailed account of the anatomy of Amphioxus as compared with that of higher Vertebrates. The third chapter deals with the embryonic and larval development of Amphioxus, while the fourth deals more briefly with the anatomy, embryology, and relationships of the Ascidians; then the other allied forms, Balanoglossus, Cephalodiscus, are described.

The work concludes with a series of discussions touching the problem proposed in the Introduction, in which it is attempted to define certain general principles of Evolution by which the descent of the Vertebrates from Invertebrate ancestors may be supposed to have taken place.

The work contains an extensive bibliography, full notes, and 135 illustrations.

TABLE OF CONTENTS.

INTRODUCTION.
CHAPTER I. ANATOMY OF AMPHIOXUS.
II. Ditto.
III. DEVELOPMENT OF AMPHIOXUS.
IV. THE ASCIDIANS.
V. THE PROTOCHORDATA IN THEIR RELATION TO THE PROBLEM OF VERTEBRATE DESCENT.

III. FISHES, LIVING AND FOSSIL.

AN INTRODUCTORY STUDY.

BY

BASHFORD DEAN, PH.D., COLUMBIA,

Instructor in Biology, Columbia University.

8vo. Cloth. $2.50, net.

This work has been prepared to meet the needs of the general student for a concise knowledge of the Fishes. It contains a review of the four larger groups of the strictly fishlike forms, Sharks, Chimaeroids, Teleostomes, and the Dipnoans, and adds to this a chapter on the Lampreys. It presents in figures the prominent members, living and fossil, of each group; illustrates characteristic structures; adds notes upon the important phases of development, and formulates the views of investigators as to relationships and descent.

The recent contributions to the knowledge of extinct Fishes are taken into special account in the treatment of the entire subject, and restorations have been attempted, as of Dinichthys, Ctenodus, and Cladoselache.

The writer has also indicated diagrammatically, as far as generally accepted, the genetic relationships of fossil and living forms.

The aim of the book has been mainly to furnish the student with a well-marked ground-plan of Ichthyology, to enable him to better understand special works, such as those of Smith Woodward and Günther. The work is fully illustrated, mainly from the writer's original pen-drawings.

TABLE OF CONTENTS.

CHAPTER

I. FISHES. Their Essential Characters. Sharks, Chimaeroids, Teleostomes, and Lung-fishes. Their Appearance in Time and their Distribution.

II. THE LAMPREYS. Their Position with Reference to Fishes. Bdellostoma, Myxine, Petromyzon, Palaeospondylus.

III. THE SHARK GROUP. Anatomical Characters. Its Extinct Members, Acanthodian, Cladoselachid, Xenacanthid, Cestracionts.

IV. CHIMAEROIDS. Structures of Callorhynchus and Chimaera. Squaloraja and Myriacanthus. Life-habits and Probable Relationships.

V. TELEOSTOMES. The Forms of Recent "Ganoids." Habits and Distribution. The Relations of Prominent Extinct Forms. Crossopterygians. Typical "Bony Fishes."

VI. THE EVOLUTION OF THE GROUPS OF FISHES. Aquatic Metamerism. Numerical Lines. Evolution of Gill-cleft Characters, Paired and Unpaired Fins, Aquatic Sense-organs.

VII. THE DEVELOPMENT OF FISHES. Prominent Features in Embryonic and Larval Development of Members of each Group. Summaries.

V. The Foundations of Zoölogy

By **WILLIAM KEITH BROOKS,**

Professor of Zoölogy, Johns Hopkins University.

8vo. Cloth. Price $2.50 *net.*

EXTRACT FROM PREFACE.

"I shall try to show that life is response to the order of nature; in fact, this thesis is the text of most of the lectures: but if it be admitted, it follows that biology is the study of response, and that the study of that order of nature to which response is made is as well within its province as the study of the living organism which responds, for all the knowledge we can get of both these aspects of nature is needed as a preparation for the study of that relation between them which constitutes life. Our interest in all branches of science is vital interest. It is only as living things that we care to know. Life is that which, when joined to mind, is knowledge, — knowledge in use; and we may be sure that all living things with minds like ours are conscious of some part of the order of nature, for the response in which life consists is response to this order. The statement that physical phenomena are natural seems to mean little, but the phenomena of life are so wonderful that many hesitate, even at the present day, to believe that nature can be such a wonderful thing as it must be if the actions of all living things are natural; and, as I shall try to find out in this course of lectures what we mean by the assertion that living nature is natural, I shall now attempt, by a few illustrations, to give a broad outline of some of the most notable features of the nature of living things."

TABLE OF CONTENTS:

I. Introductory.
II. Huxley and the Problem of the Naturalist.
III. Nature and Nurture.
IV. Lamarck.
V. Migration in its Bearing on Lamarckism.
VI. (I) Zoölogy and the Philosophy of Evolution.
VI. (II) An Inherent Error in the Views of Galton and Weismann on Inheritance.
VII. Galton and the Statistical Study of Inheritance.
VIII. Darwin and the Origin of Species.
IX. Natural Selection and the Antiquity of Life.
X. Natural Selection and Natural Theology.
XI. Paley and the Argument from Contrivance.
XII. The Mechanism of Nature.
XIII. Louis Agassiz and George Berkeley.

THE MACMILLAN COMPANY

66 FIFTH AVENUE, NEW YORK